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Soluble glass and all its applications.	Feuchtwanger, Lewis, 1805-1876.	1873.	TP869 .F42
Soluble silicates /	Falcone, James S., 1946-	1982.	TP245.S5 S6 1982
Soluble silicates, their properties and uses /	Vail, James Garrett, 1886-1951.	1952.	TP245.S5 V3
Solution to one of the most celebrated fundamental questions (hitherto unsolved) in dynamics ... / by Martin Gardiner, C. E.	Gardiner, Martin.	1883	QA871 .G2
A solution to the hidden-line problem for computer-drawn polyhedra /	Loutrel, Philippe Paul, 1942-	1967.	QA491 .L89 1967
Solutions! /	Technical Association of the Pulp and Paper Industry.		TS1080 .T3
Solutions and examples for Perl programmers	Christiansen, Tom.	c1998.	e-book
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Hydrocyclone	Bradley, D.		TP159.S4.B7
Hydrodynamic lubrication : bearings and thrust bearings /	Frène, Jeab.	1997.	TJ1073 .H93 1997
Hydrodynamics in ship design /	Saunders, Harold Eugene, 1890-1961.	1957-1965.	VM156 .S3
Hydrodynamics of unstable media : general theory and applied problems /	Trubnikov, B. A. (Boris Andreevich)	c1996.	QC174.26.W28 Z48 1996
Hydroelectric handbook /	Creager, William Pitcher, 1878-	[1950]	TK1081 .C7 1950
Hydrofluoric acid alkylation.	Phillips Petroleum Company.	[1946]	TP690.45 .P5
Hydrogels and biodegradable polymers for bioapplications /	Ottenbrite, Raphael M.	1996.	R857.P6 H96 1996
The Hydrogen bond /	Pimentel, George C.	1960.	QD471 .P5
Hydrogen compounds of the metallic elements /	Mackay, K. M. (Kenneth Malcolm)	1966.	QD181.H1 M3

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L14         11 L13 AND L12

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2004:20339 Document No.: PREV200400022212. Crystal modification C of 8-cyano-1-cyclopropyl-7-(1S,6S-2,8-diazabicyclo-[4.3. 0]nonan-8-yl)-6-fluoro-1,4-dihyro-4-oxo-3-quinoline carboxylic. **Rast, Hubert** [Inventor, Reprint Author]; **Himmler, Thomas** [Inventor]. Leverkusen, Germany. ASSIGNEE: Bayer Aktiengesellschaft, Leverkusen, Germany. Patent Info.: US 6649762 November 18, 2003. Official Gazette of the United States Patent and Trademark Office Patents, (Nov 18 2003) Vol. 1276, No. 3. http://www.uspto.gov/web/menu/patdata.html. e-file.
ISSN: 0098-1133 (ISSN print). Language: English.

AB The present invention relates to a defined crystal modification of 8-cyano-1-cyclopropyl-7-(1S,6S-2,8-diazabicyclo[4.3. 0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid of the formula (1), to processes for its preparation and to its use in pharmaceutical preparations. ##STR1## The crystal modification can be distinguished from other crystal modifications of 8-cyano-1-cyclopropyl-7-(1S,6S-2,8-diazabicyclo[4.3. 0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid of the formula (1) by its characteristic X-ray powder diffractogram and its differential thermodiagram (see description).

L14 ANSWER 2 OF 11 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

2003:68685 Document No.: PREV200300068685. Crystal modification d of 8-cyano-1-cyclopropyl-7-(1s, 6s- 2,8-diazabicyclo-[4.3.0]nonan-8-yl)-6-fluoro-1,4- dihydro-4-oxo-3-quinolinecarboxylic acid. **Himmler, Thomas** [Inventor, Reprint Author]; **Rast, Hubert** [Inventor]. Odenthal, Germany. ASSIGNEE: Bayer Aktiengesellschaft, Leverkusen, Germany. Patent Info.: US 6492391 December 10, 2002. Official Gazette of the United States Patent and Trademark Office Patents, (Dec 10 2002) Vol. 1265, No. 2. http://www.uspto.gov/web/menu/patdata.html. e-file.
ISSN: 0098-1133 (ISSN print). Language: English.

AB The present invention relates to a defined crystal modification of 8-cyano-1-cyclopropyl-7-(1S,6S-2,8-diazabicyclo[4.3. 0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid, to processes for its preparation and to its use in pharmaceutical preparations. ##STR1## The crystal modification can be distinguished from other crystal modifications of 8-cyano-1-cyclopropyl-7-(1S,6S-2,8-diazabicyclo[4.3. 0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid of the formula (I) by its characteristic X-ray powder diffractogram and its differential thermodiagram (see description).

L14 ANSWER 3 OF 11 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

2002:523331 Document No.: PREV200200523331. Crystal modification A of 8-cyano-1-cyclopropyl-7-(is,6s-2,8-diazabicyclo[4.3. 0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid. **Himmler, Thomas** [Inventor, Reprint author]; Hallenbach, Werner [Inventor]; **Rast, Hubert** [Inventor]. Odenthal, Germany. ASSIGNEE: Bayer Aktiengesellschaft, Leverkusen, Germany. Patent Info.: US 6436955 August 20, 2002. Official Gazette of the United States Patent and Trademark Office Patents, (Aug. 20, 2002) Vol. 1261, No. 3. http://www.uspto.gov/web/menu/patdata.html. e-file.
CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

AB The present invention relates to a defined crystal modification of 8-cyano-1-cyclopropyl-7-(1S,6S-2,8-diazabicyclo[4.3.0] nonan-8-yl)-6-fluoro-1, 4-dihydro-4-oxo-3-quinolinecarboxylic acid of the formula (I), to processes for its preparation and to its use in

pharmaceutical preparations. ##STR1## The crystal modification can be distinguished from other crystal modifications of 8-cyano-1-cyclopropyl-7-(1S,6S-2,8-diazabicyclo[4.3.0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid of the formula (I) by its characteristic X-ray powder diffractogram and its differential thermodiagram (see description).

L14 ANSWER 4 OF 11 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

2002:72624 Document No.: PREV200200072624. Possibly substituted 8-cyano-1-cyclopropyl-7-(2,8-diazabicyclo-[4.3. 0]-nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolin carboxylic acids and their derivatives. Bartel, Stefan [Inventor, Reprint author]; Jaetsch, Thomas [Inventor]; **Himmler, Thomas** [Inventor]; **Rast, Hans-Georg** [Inventor]; Hallenbach, Werner [Inventor]; Heinen, Ernst [Inventor]; Pirro, Franz [Inventor]; Scheer, Martin [Inventor]; Stegemann, Michael [Inventor]; Stupp, Hans-Peter [Inventor]; Wetzstein, Heinz-Georg [Inventor]. Bergisch Gladbach, Germany. ASSIGNEE: Bayer Aktiengesellschaft, Leverkusen, Germany. Patent Info.: US 6323213 November 27, 2001. Official Gazette of the United States Patent and Trademark Office Patents, (Nov. 27, 2001) Vol. 1252, No. 4. ftp://ftp.uspto.gov/pub/patdata/. e-file. CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

AB The present invention relates to novel optionally substituted 8-cyano-1-cyclo-propyl-7-(2,8-diazabicyclo[4.3. 0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acids and their derivatives, of the general formula (I) ##STR1## in which R1 represents hydrogen, C1 -C4 -alkyl which is optionally substituted by hydroxyl, methoxy, amino, methylamino or dimethylamino, or (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl, R2 represents hydrogen, benzyl, C1 -C3 -alkyl, (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl, radicals having the structures --CHdbdCH--COOR3, --CH2 CH2 COOR3, --CH2 CH2 CN, --CH2 CH2 COCH3 or --CH2 COCH3, in which R3 represents methyl or ethyl, or a radical of the general structure R4 --(NH--CHR5 --CO)n --, in which R4 represents hydrogen, C1 -C3 -alkyl or the radical --COO-tert-butyl, R5 represents hydrogen, C1 -C4 -alkyl, hydroxyalkyl, aminoalkyl, thioalkyl, carboxyalkyl or benzyl and n is 1 or 2, and Y is oxygen or sulfur, the process for their preparation and their use in antibacterial compositions.

L14 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

2000:607382 Document No. 133:213147 Crystal modification C of 8-cyano-1-cyclopropyl-7-[(1S,6S)-2,8-diazabicyclo[4.3.0]nonan-8-yl]-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid. **Rast, Hubert; Himmler, Thomas** (Bayer A.-G., Germany). Ger. Offen. DE 19908449 A1 20000831, 12 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1999-19908449 19990226.

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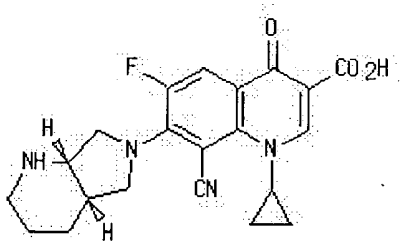

I

h eb c g cg b cg eb

AB The title compd. (I) is converted to stable crystal modification C (m. 235-237°) by holding I at room temp. and relative humidity ≥92% until no further wt. gain occurs, drying, and heating to above the conversion temp. (150-180°). I modification D is characterized by its powder x-ray diffractogram, IR spectrum, and by DTA. I is highly active against pathogenic bacteria in human and veterinary medicine.

L14 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

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2000:607381 Document No. 133:213146 Crystal modification D of 8-cyano-1-cyclopropyl-7-[(1S,6S)-2,8-diazabicyclo[4.3.0]nonan-8-yl]-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid. **Himmler, Thomas; Rast, Hubert** (Bayer A.-G., Germany). Ger. Offen. DE 19908448 A1 20000831, 12 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1999-19908448 19990226.

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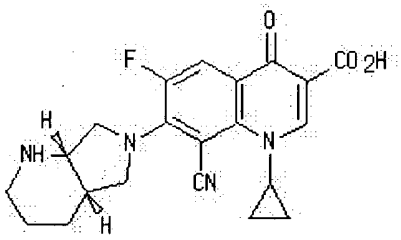

I

AB The title compd. (I) is converted to stable crystal modification D (m. 261-265°) by dissolving I in H2O to a concn. of 1-3 wt.%, allowing the soln. to stand until a ppt. forms, removing the ppt. by filtration, drying the remaining soln., and heating the solid obtained to above the transition temp. (130-160°). I modification D is characterized by its powder x-ray diffractogram, IR spectrum, and by DTA. I is highly active against pathogenic bacteria in human and veterinary medicine.

L14 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

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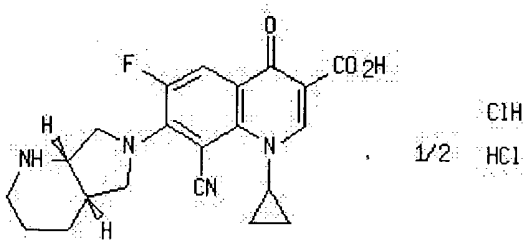
2000:366037 Document No. 133:4647 Semihydrochloride of 8-cyano-1-cyclopropyl-7-(1S,6S-2,8-diazabicyclo[4.3.0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid. **Himmler, Thomas; Rast, Hubert** (Bayer A.-G., Germany). Ger. Offen. DE 19854357 A1 20000531, 16 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1998-19854357 19981125.

GI



I

AB The title compd. (I), useful as a medical and veterinary bactericide, shows good water soly. (19 wt.%). I is produced by reaction of 7-halo-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-

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quinolinecarboxylic acid with (1S,6S)-2,8-diazabicyclo[4.3.0]nonane in the presence of a base in one of the following diluents: (a) a C≥4 aliph. alc., (b) a mixt. of a C>3 alc. with the polar aprotic diluent, N-methylpyrrolidone; (c) a mixt. of n-PrOH with DMF. I (m. 278-280°) is characterized by its powder x-ray diffractogram, differential thermogram, and IR spectrum.

L14 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

Check References

2000:366036 Document No. 133:4646 Crystal modification A of 8-cyano-1-cyclopropyl-7-(1S,6S-2,8-diazabicyclo[4.3.0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid. **Himmler, Thomas;** Hallenbach, Werner; **Rast, Hubert** (Bayer A.-G., Germany). Ger. Offen. DE 19854356 A1 20000531, 8 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1998-19854356 19981125.

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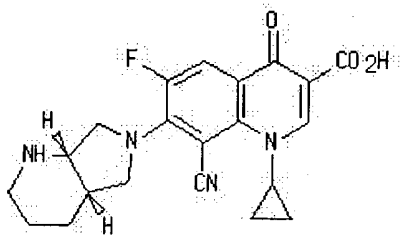

I

AB The title compd. in crystal modification A (I), useful as a medical and veterinary bactericide, is stable during extended storage without conversion to the amorphous form or any other crystal modification, and is less hygroscopic than the amorphous form of the compd. I is produced by dissolving the amorphous compd. or an unknown modification of it in hot water or a hot water-alc. mixt., adding an alc. (esp. EtOH or iso-PrOH), and cooling to room temp. I (m. 249-252°) is characterized by its powder x-ray diffractogram, differential thermogram, and IR spectrum.

L14 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

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2000:366035 Document No. 133:4645 Crystal modification B of 8-cyano-1-cyclopropyl-7-(1S,6S-2,8-diazabicyclo[4.3.0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid. **Himmler, Thomas;** Hallenbach, Werner; **Rast, Hubert** (Bayer A.-G., Germany). Ger. Offen. DE 19854355 A1 20000531, 8 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1998-19854355 19981125.

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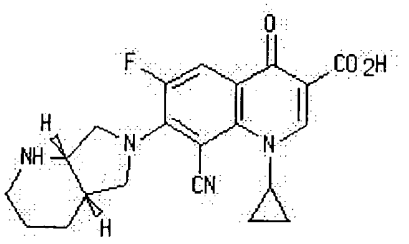

I

AB The title compd. in crystal modification B (I), useful as a medical and

h eb c g cg b cg eb

veterinary bactericide, is stable during extended storage without conversion to the amorphous form or any other crystal modification, and is less hygroscopic than the amorphous form of the compd. I is produced either (a) by reaction of 7-halo-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid with (1S,6S)-2,8-diazabicyclo[4.3.0]nonane in the presence of a base in a mixt. of EtOH and a polar aprotic diluent such as N-methylpyrrolidone, DMF, or sulfolane, or (b) by heating an unknown modification of the compd. in the presence of a base in EtOH, n-PrOH, iso-PrOH, or a mixt. of one of these alcs. with one of the polar aprotic diluents named previously. I (m. 243-245°) is characterized by its powder x-ray diffractogram, differential thermogram, and IR spectrum.

L14 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

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1998:38463 Document No. 128:102103 Preparation of 7-(3-vinylpiperazin-1-yl)quinolonecarboxylic acids as antibacterials.. **Himmler, Thomas**; Jaetsch, Thomas; Hallenbach, Werner; **Rast, Hans-Georg**; Wetzstein, Heinz-Georg; Heinen, Ernst; Pirro, Franz; Scheer, Martin; Stegemann, Michael; Stupp, Hans-Peter (Bayer A.-G., Germany). Ger. Offen. DE 19651687 A1 19980102, 16 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1996-19651687 19961212. PRIORITY: DE 1996-19625988 19960628.

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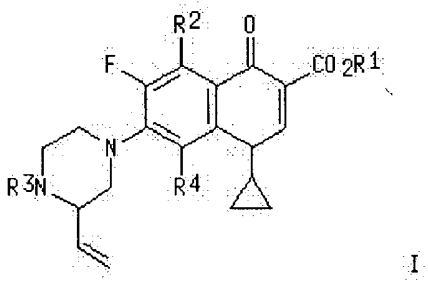

I

AB Title compds. [I; R1 = H, (substituted) alkyl; R2 = H, F, amino, Me, vinyl; R3 = H, PhCH2, alkyl, CH2CH2CN, CH2COMe, etc.; R4 = H, F, Cl, OMe, F2CHO, cyano, ethynyl], were prepd. Thus, 8-chloro-1-cyclopropyl-6,7-difluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid, 2-vinylpiperazine, and DABCO were refluxed in MeCN/DMF to give 52% 8-chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(3-vinylpiperazin-1-yl)-3-quinolinecarboxylic acid. The latter showed ED90 = 1.25 mg/kg orally against E. coli 6200 in chickens.

L14 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

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1997:579724 Document No. 127:248093 8-Cyano-1-cyclopropyl-7-(2,8-diazabicyclo[4.3.0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid derivatives. Bartel, Stefan; Jaetsch, Thomas; **Himmler, Thomas**; **Rast, Hans-Georg**; Hallenbach, Werner; Heinen, Ernst; Pirro, Franz; Scheer, Martin; Stegemann, Michael; Stupp, Hans-Peter; Wetzstein, Heinz-Georg (Bayer A.-G., Germany; Bartel, Stefan; Jaetsch, Thomas; Himmler, Thomas; Rast, Hans-Georg; Hallenbach, Werner; Heinen, Ernst; Pirro, Franz; Scheer, Martin; et al.). PCT Int. Appl. WO 9731001 A1 19970828, 36 pp. DESIGNATED STATES: W: AU, BB, BG, BR, BY, CA, CN, CZ, HU, IL, JP, KR, KZ, LK, MX, NO, NZ, PL, RO, RU, SK, TR, UA, US; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (German). CODEN: PIXXD2.

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APPLICATION: WO 1997-EP637 19970212. PRIORITY: DE 1996-19606762 19960223; DE 1996-19633805 19960822.

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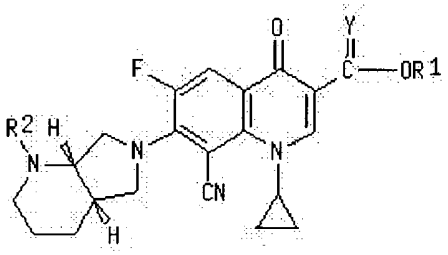

I

AB Title compds. I [R1 = H, alkyl, optionally substituted by OH, OMe, NH2, NHMe, NMe2, or (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl; R2 = H, benzyl, alkyl, (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl, CH=CHCO2R3, CH2CH2CO2R3, CH2CH2CN, CH2CH2COMe, CH2COMe; R3 = Me, Et, R4(NHCHR5CO)n; R4 = H, alkyl, CO2CMe3; R5 = H, alkyl, hydroxyalkyl, aminoalkyl, thioalkyl, carboxyalkyl, benzyl; n = 1, 2; Y = O, S] were prepd. for use as antibacterial agents. Thus, I [R1 = OH, R2 = H, Y = O] was prepd. by aminating the 7-chloroquinoline. I [R1 = OH, R2 = H, Y = O] had min. inhibitory concns. against a no. of bacteria that were superior to those of enrofloxacin.

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=> s salt? () formation
L1          8396 SALT? (W) FORMATION

=> s solubility
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L2      336437 SOLUBILITY

=> s l1 and l2
L3          458 L1 AND L2

=> s l3 and review
L4           21 L3 AND REVIEW

=> s l4 and hydrochloride
L5            0 L4 AND HYDROCHLORIDE

=> s l4, cbib abs, 1-21
L6            0 L4, CBIB ABS, 1-21

=> d l3, cbib abs, 1-21

L3   ANSWER 1 OF 458     MEDLINE on STN
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2004259732. PubMed ID: 15158947. Modification of physicochemical and mechanical properties of shellac by partial hydrolysis. Limmatvapirat Sontaya; Limmatvapirat Chutima; Luangtana-Anan Manee; Nunthanid Jurairat; Oguchi Toshio; Tozuka Yuichi; Yamamoto Keiji; Puttipipatkhachorn Satit. (Department of Pharmaceutical Technology, Faculty of Pharmacy, Silpakorn University, Nakhon Pathom 73000, Thailand.) International journal of pharmaceutics, (2004 Jun 18) 278 (1) 41-9. Journal code: 7804127. ISSN: 0378-5173. Pub. country: Netherlands. Language: English.

AB The shellac was modified by partial hydrolysis with 2.0% (w/w) NaOH for different times. The hydrolysed shellac was then evaluated for physicochemical and film properties in comparison with native shellac. The tablets coated with native and hydrolysed shellac were also evaluated. The results demonstrated that acid value (AV) of shellac increased with prolongation of hydrolysis time. The **solubility** of shellac in buffer solution (pH < or = 7) gradually increased with increasing hydrolysis time. The films prepared from hydrolysed shellac were more flexible and soft than those prepared from native shellac. The increasing of flexibility was correlated with the increasing of soft resin in shellac. The water vapor permeability of hydrolysed shellac film was lower than that of native shellac film. The higher acid permeability of the tablet coated with hydrolysed shellac was observed. In ethanol-based film coating, shellac had lower **solubility** and thus lower drug dissolution from coated tablets was observed. In ammonia-based film coating, the **solubility** of shellac was improved higher nearby pH 7.0 by an ammonium neutralisation method because of forming well-soluble salts, thereby higher drug dissolution was obtained. Partial hydrolysis provided modified shellac, which is more effective for ammonium **salt formation**, thus very higher drug dissolution was achieved in the ammonia-based coated tablets.


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L3   ANSWER 2 OF 458     MEDLINE on STN
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2004109692. PubMed ID: 14962584. Impact of solid state properties on developability assessment of drug candidates. Huang Lian-Feng; Tong Wei-Qin. (Johnson & Johnson Pharmaceutical Research and Development, L.L.C., 1000 Route 202, Raritan, NJ 08869, USA.. weiqin.tong@pharma.norvartis.com) . Advanced drug delivery reviews, (2004 Feb 23) 56 (3) 321-34. Ref: 43. Journal code: 8710523. ISSN: 0169-409X. Pub. country: Netherlands. Language: English.

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AB Solid state properties including polymorphism, solvate and **salt formation** can have a profound impact on two of the most important properties that are essential to the successful development of drug candidates: **solubility** and stability. To enable meaningful evaluations of drug candidates for their development risks, often referred to as developability, and provide input to the molecular design regarding the "drug-like" properties, one must take into account the impact of solid state properties on **solubility** and stability. This review examines the importance of solid state properties and their relationship to developability criteria. Phase appropriate characterization strategies and appropriate salt and crystal form screening and selection processes are discussed. These strategies and processes should balance the need for speed and throughput of modern discovery with the quality of data essential to the adequate developability assessment. Specific examples are given to illustrate the importance of understanding the solid state properties and their impact on developability.

L3 ANSWER 3 OF 458 MEDLINE on STN

2004029824. PubMed ID: 14730370. Improving the aqueous **solubility** of triclosan by solubilization, complexation, and in situ **salt formation**. Grove Christine; Liebenberg Wilna; du Preez Jan L; Yang Wenzhan; de Villiers Melgardt M. (School of Pharmacy, Potchefstroom University for Christian Higher Education, Potchefstroom 2520, South Africa.) Journal of cosmetic science, (2003 Nov-Dec) 54 (6) 537-50. Journal code: 9814276. ISSN: 1525-7886. Pub. country: United States. Language: English.

AB Triclosan, an antimicrobial, although widely incorporated into many skin care products, toothpastes, and liquid soaps, presents formulation difficulties because it is practically insoluble in water. The objective of this study was to improve the aqueous **solubility** of triclosan through solubilization, complexation, and **salt formation**. The **solubility** of triclosan in distilled water and in phosphate buffers (pH 7.4) was determined at 30 degrees C. The order of solubilizing performance of the solubilizers was: N-methylglucamine> or =L-arginine>sodium lauryl sulfate>beta-cyclodextrin> or =hydroxypropyl-beta-cyclodextrin>ethanolamine>sodium benzoate>sodium methyl 4-hydroxybenzoate>triethanolamine> or =diethanolamine. These solubilizers increased the **solubility** of triclosan from 80- to 6000-fold. Micellar solubilization and the formation of either salts or complexes are postulated as possible mechanisms for the increase in the **solubility** of triclosan by the surfactant sodium lauryl sulphate, the cyclic sugar derivatives beta-cyclodextrin and 2-hydropropyl-beta-cyclodextrin, the amino acid L-arginine, and the amino sugar alcohol N-methylglucamine. Furthermore, although the bacteriostatic efficacy of triclosan was significantly increased when solubilized with N-methylglucamine, L-arginine, and ethanolamine, increased solubilization did not increase the effectiveness of triclosan for all solubilizers tested.

L3 ANSWER 4 OF 458 MEDLINE on STN

2003323560. PubMed ID: 12852955. Design and synthesis of poly(ADP-ribose)polymerase-1 (PARP-1) inhibitors. Part 3: In vitro evaluation of 1,3,4,5-tetrahydro-benzo[c][1,6]- and [c][1,7]-naphthyridin-6-ones. Ferraris Dana; Ficco Rica Pargas; Pahutski Thomas; Lautar Susan; Huang Shirley; Zhang Jie; Kalish Vincent. (Guilford Pharmaceuticals Inc., 6611 Tributary Street, Baltimore, MA 21224, USA.. ferrarisd@guilfordpharm.com) . Bioorganic & medicinal chemistry letters, (2003 Aug 4) 13 (15) 2513-8. Journal code: 9107377. ISSN: 0960-894X. Pub.

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country: England: United Kingdom. Language: English.

AB The 1,3,4,5-tetrahydro-benzo[c][1,6]- and [c][1,7]-napthyridin-6-ones are presented as a potent class of PARP-1 inhibitors. Derivatives of these partially saturated aza-5[H]-phenanthridin-6-ones were designed and synthesized with tertiary amines for **salt formation**, thus enhancing aqueous **solubility**, iv formulation and their potential use in acute ischemic injuries (i.e., myocardial ischemia and stroke). We found that partial saturation of the C-ring results in derivatives that are several times more potent than the aromatic C-ring derivatives. The general synthetic routes are presented herein as well as thorough in vitro potencies and SAR discussion for selected derivatives.

L3 ANSWER 5 OF 458 MEDLINE on STN

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2003083024. PubMed ID: 12593936. Effect of buffer media composition on the **solubility** and effective permeability coefficient of ibuprofen. Levis Karl A; Lane Majella E; Corrigan Owen I. (Department of Pharmaceutics and Pharmaceutical Technology, School of Pharmacy, Trinity College Dublin, Dublin 2, Ireland.) International journal of pharmaceutics, (2003 Mar 6) 253 (1-2) 49-59. Journal code: 7804127. ISSN: 0378-5173. Pub. country: Netherlands. Language: English.

AB The effect of perfusion medium composition on the two important biopharmaceutical parameters drug **solubility** and permeability was determined for ibuprofen. Eight commonly used buffers were examined. Equilibrium **solubility**, buffer capacity profiles and permeability coefficients, using the in situ rat gut perfusion model, were determined for each medium at 37 degrees C. The **solubility** of ibuprofen differed sixfold over the range of buffer systems studied. The differences in **solubility** were associated with different pHs of the buffers when saturated with drug and also the presence of micelles and divalent ions. The **solubility** of ibuprofen in FeSSIF was significantly higher than predicted from the pH due to micellisation, while that in Krebs was significantly lower due to ibuprofen-calcium **salt formation**. Buffer capacities varied over a 40-fold range. The pK(a) values of the buffer components were determined from the buffer capacity versus pH profiles and were in good agreement with the thermodynamic values when corrected for temperature and ionic strength. Smaller, but statistically significant differences in P(app) values for ibuprofen were also observed between some of the buffers. During perfusion, pHs of the perfusate samples gradually changed over time towards a median value of approximately 6.5. HBSS gave a P(app) approximately 50% greater than that observed in PBS 7.4. Physicochemical factors such as medium pH, buffer capacity and osmolarity should be considered when determining the P(app) values of ionisable compounds. Care needs to be exercised when comparing P(app) values from different laboratories as buffer composition can have a significant effect on both **solubility** and permeability of a drug, whose ionisation is substantially changed over the pH range of the buffers. Despite the high amount ionised, ibuprofen appears to be well absorbed and it can be classified as a highly permeable drug.

L3 ANSWER 6 OF 458 MEDLINE on STN

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2002643809. PubMed ID: 12403076. Enhanced percutaneous absoption of piroxicam via **salt formation** with ethanolamines. Cheong Hyun-Ah; Choi Hoo-Kyun. (College of Pharmacy, Chosun University, Gwangju, Korea.) Pharmaceutical research, (2002 Sep) 19 (9) 1375-80. Journal code: 8406521. ISSN: 0724-8741. Pub. country: United States. Language: English.

AB PURPOSE: The aim of this work was to prepare piroxicam-ethanolamine salts

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(PX-EAs) with improved physicochemical properties for transdermal application. METHODS: The physicochemical properties of prepared salts were investigated by DSC and FT-IR. Their percutaneous absorption characteristics across hairless mouse skin and the effect of various enhancers were studied using a flow-through diffusion cell system. RESULTS: Three piroxicam-ethanolamine salts were prepared. Piroxicam monoethanolamine salt (PX-MEA) and piroxicam diethanolamine salt (PX-DEA) had higher **solubility** than piroxicam in most of vehicles tested and a higher permeation rate across the skin. The **solubility** and permeation rate of piroxicam triethanolamine salt (PX-TEA) was lower than those of piroxicam in most of vehicles tested. However, there was no significant change in octanol/water partition coefficient by **salt formation**. **Salt formation** lowered the melting point of piroxicam and, of the systems examined, PX-DEA showed the lowest melting point. When the effect of various enhancers were evaluated, nonionic surfactants having medium HLB, an alkyl chain length of C18 and an ethylene oxide chain were better able to modify the permeability of the stratum corneum and to promote the effective penetration of piroxicam and PX-EAs. CONCLUSIONS: Piroxicam **salt formation** with MEA and DEA improved the physicochemical properties and enhanced the skin permeability of piroxicam.

L3 ANSWER 7 OF 458 MEDLINE on STN

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2002357184. PubMed ID: 12100849. Physicochemical properties of amorphous salt of cimetidine and diflunisal system. Yamamura Shigeo; Gotoh Hiroaki; Sakamoto Yohko; Momose Yasunori. (School of Pharmaceutical Sciences, Toho University, Miyama 2-2-1, Funabashi, Chiba 274-8510, Japan.. yamamura@phar.toho-u.ac.jp) . International journal of pharmaceutics, (2002 Jul 25) 241 (2) 213-21. Journal code: 7804127. ISSN: 0378-5173. Pub. country: Netherlands. Language: English.

AB The purpose of this study was to prepare amorphous precipitates of the binary system of cimetidine (CIM) and diflunisal (DIF) and to investigate the physicochemical properties of the precipitates. To achieve this, the interaction between CIM and DIF molecules was studied by means of nuclear magnetic resonance (NMR) and Fourier-transform infrared (FTIR) measurements. The binary system of CIM and DIF was found to become amorphous upon precipitation from ethanol solution, without heating or melting. In the thermal analysis by TG-DTA equipped with a mass spectrometer, decarboxylation of DIF was found to occur below its melting temperature. In NMR studies, the chemical shifts of a proton in the imidazole ring of CIM and the carbon to which the DIF carboxyl group is bound were found to change depending on the composition of the binary system. The change in NMR chemical shifts suggested that a salt was formed between CIM and DIF. The precipitates had higher **solubility** than intact drugs due to this **salt formation**. The results suggest that CIM may be useful as an amorphous carrier, without requiring heating or melting, due to the formation of a salt with acidic drugs.

L3 ANSWER 8 OF 458 MEDLINE on STN

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AB The objective of this mini-review is to summarize the findings concerning

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the physicochemical properties and the pharmaceutical applications of acidic drugs whose performances have been modified by simultaneous complexation with cyclodextrins and **salt formation**. Particular attention is paid to the approaches undertaken for increasing the **solubility** of the drugs by proper choice of the type of counterion analogously to what has been reported for complexes of basic drugs in the presence of hydroxy acids.

L3 ANSWER 9 OF 458 MEDLINE on STN

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2001366655. PubMed ID: 11427358. Comparison of the physicochemical properties of the N-(2-hydroxyethyl) pyrrolidine, diethylamine and sodium salt forms of diclofenac. O'Connor K M; Corrigan O I. (Department of Pharmaceutics and Pharmaceutical Technology, School of Pharmacy, Trinity College, 2, Dublin, Ireland.) International journal of pharmaceutics, (2001 Jul 17) 222 (2) 281-93. Journal code: 7804127. ISSN: 0378-5173. Pub. country: Netherlands. Language: English.

AB Non steroidal anti-inflammatory agents (NSAIDs) such as diclofenac have very low aqueous **solubilities** and consequently **salt formation** may be used to enhance **solubility** and dissolution rate. In this study, we examined the physicochemical properties of three diclofenac salts, diclofenac sodium (DNa), diclofenac N-(2-hydroxyethyl)pyrrolidine (DHEP) and diclofenac diethylamine (DDEA), and their different solid state forms to determine the influence of salt form on **solubility**, dissolution rate and membrane transport. The equilibrium **solubility** of DDEA at 25 degrees C was determined as 33 mM, lower than the **solubilities** of DHEP (273 mM) and DNa (66 mM) previously reported (Ledwidge and Corrigan, 1998). In addition to the dihydrate form of DHEP previously characterised, monohydrate forms of DHEP and DDEA were identified. Intrinsic dissolution rate studies were used to determine the **solubility** ratios of the hydrated and anhydrous forms. The monohydrate form of DHEP was found to be 1.8 times less soluble than the anhydrate, whereas DDEA anhydrate was approximately 1.7 times as soluble as the monohydrate form. On investigation of the pH-**solubility** profile (25 degrees C) of DDEA, appreciable supersaturation (76 mM) relative to the theoretical profile, was detected at the pH(max). This contrasts with values of >800 and 67 mM for DHEP and DNa, respectively. The transport of salt solutions through a porous membrane (Visking) was investigated. A linear relationship between concentration (mM) and rate of transport (mmol/h) was established for DNa and DHEP solutions. The mass transfer coefficient determined for DHEP was lower than that for the other two salts. Nevertheless, the maximum transport rate obtained for DHEP is almost six times higher than that obtained for DDEA.

L3 ANSWER 10 OF 458 MEDLINE on STN

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AB A series of four beta-cyclodextrin complexes (called products) was formed by neutralizing an acidic drug to study the effect of drug **solubility** on complex formation and the dissolution performance from direct compression tablets. Four solid products were prepared by neutralizing the drug in

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0.05, 0.10, 0.20, and 0.30 M tromethamine solutions with a constant 0.09 M beta-cyclodextrin concentration, filtering the solutions, and removing the water through evaporation with heat and vacuum. The four products contained drug and water in a distinct relationship, thus suggesting a complex formation that was dependent on the tromethamine concentration. Infrared, powder X-ray diffraction, differential scanning calorimetry (DSC), phase **solubility**, and scanning electron microscopy (SEM) techniques revealed distinct differences among the four products, suggesting three of the four products were complexes, and one product was either a weak complex or a physical mixture. Ultraviolet (UV) analysis showed no evidence of complex formation. Phase **solubility** results showed one product had a slight increase in drug **solubility**, and three products had no increase in drug **solubility** with increasing beta-cyclodextrin concentration. The lack of a **solubility** increase suggests insoluble complex formation. Drug dissolution in water was improved significantly in all tablets containing either a product or a physical mixture when compared to the pure drug. The products prepared with the two highest concentrations of tromethamine showed a dissolution performance that was superior to all other formulations. Enthalpy measurements by DSC were a good indicator of dissolution performance for tablets containing the four products. Drug dissolution through **salt formation** in the absence of beta-cyclodextrin showed the drug-salt dissolution varied from better to worse when compared to the dissolution profiles of the four products. The varying dissolution performance was attributed to the formation of distinct beta-cyclodextrin complexes with varing **solubilities**.

L3 ANSWER 11 OF 458 MEDLINE on STN

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2000256925. PubMed ID: 10794696. Protease inhibitors: synthesis and QSAR study of novel classes of nonbasic thrombin inhibitors incorporating sulfonylguanidine and O-methylsulfonylisourea moieties at P1. Supuran C T; Scozzafava A; Briganti F; Clare B W. (Laboratorio di Chimica Inorganica e Bioinorganica, Universita degli Studi, Via Gino Capponi 7, I-50121 Florence, Italy.. cts@bio.chim.unifi.it) . Journal of medicinal chemistry, (2000 May 4) 43 (9) 1793-806. Journal code: 9716531. ISSN: 0022-2623. Pub. country: United States. Language: English.

AB Using benzamidine as a lead molecule, two series of alkyl/aralkyl/arylsulfonylguanidines/sulfonyl-O-methylisoureas+ ++ have been prepared and assayed as inhibitors of two serine proteases, thrombin and trypsin. The study showed that sulfaguanidine and its corresponding O-methylisourea derivative possess moderate but intrinsically selective thrombin inhibitory properties, with K(I)'s around 100 nM against thrombin and 1350-1500 nM against trypsin. Further elaboration of these two molecules afforded compounds that inhibited thrombin with K(I)'s in the range of 12-50 nM, whereas affinity for trypsin remained relatively low. Such compounds were obtained by attaching benzyloxycarbonyl- or 4-toluenesulfonylureido-protected amino acids (such as L- and D-Phe or L-Pro) or dipeptides (such as Phe-Pro, Gly-His, beta-Ala-His, or Pro-Gly) to the two leads mentioned above, sulfaguanidine and 4-aminobenzenesulfonyl-O-methylisourea. Thus, the present study proposes two novel approaches for the preparation of high-affinity, specific thrombin inhibitors: two novel S1 anchoring moieties in the already large family of arginine/amidine-based inhibitors and novel peptidomimetic scaffolds obtained by incorporating tosylureido amino acids in the hydrophobic binding site(s). The first one is important for obtaining bioavailable thrombin inhibitors, devoid of the high basicity of the commonly used arginine/amidine-based inhibitors, whereas the second one may lead to improved water **solubility** of such compounds due to

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facilitated metal (sodium) **salts formation** (at the relatively acidic SO(2)NHCO protons) as well as increased stability at hydrolysis (in vivo). A QSAR study also explained the activity in terms of global properties of the molecules, electronic properties of the sulfonylguanidine/sulfonylisou rea moiety, and novel descriptors, the frontier orbital phase angles (FOPA), that account for the directions of the nodes in the pi orbitals in the aromatic portion of those of the drugs in which the sulfonyl group was bound to a benzene ring. For thrombin inhibition, the size of the molecule was the dominant influence, while for trypsin inhibition the FOPA was the principal determinant of activity. The dependence of activity on the FOPA variables is perhaps the clearest example of a quantum effect in pharmacology and suggests a promising new tool for drug design.

L3 ANSWER 12 OF 458 MEDLINE on STN

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AB The objective of this mini-review is to summarize the findings concerning the properties and the pharmaceutical applications of multicomponent complexes made of a sparingly water-soluble amino-type drug, a cyclodextrin, and a hydroxy carboxylic acid. Simultaneous complexation and **salt formation** with these acids significantly increase the solubilizing power, allowing us to reduce the amount of cyclodextrin necessary for making the targeted formulation. In many cases, the aqueous **solubility** of the hydrophobic drug can be enhanced by several orders of magnitude, while that of CD can be enhanced more than 10-fold. The mechanism through which these complexes elicit their synergetic effects on the drug **solubility** is also discussed. Finally, some general observations are made concerning the structural requirements of the drug necessary for exploiting the aforementioned effect.
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2000070677. PubMed ID: 10601726. Investigation of the in vitro release of gentamicin from a polyanhydride matrix. Stephens D; Li L; Robinson D; Chen S; Chang H; Liu R M; Tian Y; Ginsburg E J; Gao X; Stultz T. (Advanced Drug Delivery, Hospital Products Division, Abbott Laboratories, Department 97d, 100 Abbott Park Road, Abbott Park, IL, USA.. stephend@hpd.abbott.com) . Journal of controlled release : official journal of the Controlled Release Society, (2000 Feb 3) 63 (3) 305-17. Journal code: 8607908. ISSN: 0168-3659. Pub. country: Netherlands. Language: English.

AB Septacin trade mark omitted is a sustained release formulation consisting of gentamicin sulfate dispersed in a biodegradable polyanhydride matrix. The polyanhydride matrix is a copolymer of erucic acid dimer (EAD) and sebacic acid in a 1:1 weight ratio. In vitro drug release was performed in both water and pH 7.4 phosphate buffer. The drug release in water was faster than that in the buffer, which was the opposite of what would be expected based upon a faster polymer hydrolysis rate in the buffer. Theoretical treatment of the data using the Peppas model revealed that release in water was anomalous, while the release in pH 7.4 phosphate buffer was diffusion-controlled. Profound bead morphology differences were observed between beads in these two in vitro release media. Cracking

was observed in beads in water and swelling with no apparent cracking was seen in beads in buffer. Concurrent monitoring of drug and sebacic acid release indicated that drug release is not via surface erosion. Osmotic effects were found to play little role in the in vitro drug release. There was no spectroscopic evidence of amide formation between the drug and copolymer. Sulfate release was monitored along with drug release and the results indicate that there is ion-exchange occurring during the pH 7.4 in vitro release. It was subsequently demonstrated that gentamicin can form an insoluble salt with EAD. This **salt formation** explains the slower drug release in pH 7.4 phosphate buffer.

L3 ANSWER 14 OF 458 MEDLINE on STN

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1998317646. PubMed ID: 9653759. In situ salt screening--a useful technique for discovery support and preformulation studies. Tong W Q; Whitesell G. (Glaxo Wellcome Inc., Department of Pharmaceutics, Research Triangle Park, North Carolina 27709, USA.. WT14313@glaxo.com) . Pharmaceutical development and technology, (1998 May) 3 (2) 215-23. Journal code: 9610932. ISSN: 1083-7450. Pub. country: United States. Language: English.

AB The purpose of this paper was to present an in situ salt screening technique which is applicable to most basic compounds. The theoretical aspects, experimental details, applications, and significance of this technique are illustrated through in situ salt screening studies performed on GW1818, an alpha 1A andrenergic receptor antagonist intended for treatment of benign prostatic hyperplasia (BPH). Generally, the in situ salt screening technique includes (i) acid selection, (ii) a **solubility** study, (iii) characterization of residual solids, and (iv) calculation of the Ksp and **solubility** of the salts. Six acids were screened for **salt formation** with GW1818. Excellent agreement was found between the **solubility** results determined using the authentic salts and **solubility** results obtained through in situ screening. Additional evidence of **salt formation** and some solid state properties of the salts formed in situ were obtained through microscopic examinations, differential scanning calorimetry (DSC), and x-ray powder diffraction studies. Four salts of GW1818, the phosphate, succinate, mesylate, and hydrochloride, were crystalline and demonstrated adequate **solubility**. These were selected for further evaluation. Adequate **solubility** was also observed in the case of citrate and tartrate salts, but these were considered only as potential backup candidates because they were difficult to crystallize. The results of the in situ salt screening experiments also led to the development of an IV formulation for use in pilot toxicological studies and pharmacological studies. In conclusion, the in situ salt screening technique offers a time- and compound-conserving approach for prioritizing salt selection and for providing **solubility** and stability information useful for formulation development both in the research and the development stages.

L3 ANSWER 15 OF 458 MEDLINE on STN

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95190765. PubMed ID: 7884662. Solubilization of nicardipine hydrochloride via complexation and **salt formation**. Maurin M B; Rowe S M; Koval C A; Hussain M A. (DuPont Merck Pharmaceutical Company, Wilmington, DE 19880-0336.) Journal of pharmaceutical sciences, (1994 Oct) 83 (10) 1418-20. Journal code: 2985195R. ISSN: 0022-3549. Pub. country: United States. Language: English.

AB The **solubility** behavior of nicardipine (1,4-dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridinedicarboxylic+ ++ acid methyl 2-[methyl(phenyl-methyl)amino]ethyl diester), a calcium channel blocker, used in the

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treatment of chronic stable angina and mild essential hypertension was investigated. Two techniques that are known to improve **solubility**, complexation and **salt formation**, were examined. Concentrations were determined with a specific reversed-phase HPLC assay. The **solubility** of nicardipine hydrochloride was enhanced exponentially via complexation with aliphatic carboxylic acid buffer systems in a pH dependent fashion. The **solubility** increased from 5 to 68.6 and 270 mg/mL as the acetate or propionate buffer concentrations, respectively, increased from 0.001 to 5 M, showing a positive deviation from linearity. The conversion of nicardipine hydrochloride to the phosphate salt resulted in a approximately 10-fold **solubility** improvement. The surface tension of the nicardipine phosphate in water as a function of concentration indicated a critical micelle concentration of 5-6 mg/mL. The critical micelle concentration was greater than the equilibrium **solubility** of the hydrochloride salt in water, suggesting that a self-association phenomena is responsible for the enhanced **solubility** of the phosphate salt. Both routes provided potential alternatives for the solubilization of nicardipine.

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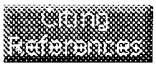

92341341. PubMed ID: 1321911. Inhibitors of blood platelet cAMP phosphodiesterase. 3. 1,3-Dihydro-2H-imidazo[4,5-b]quinolin-2-one derivatives with enhanced aqueous **solubility**. Meanwell N A; Dennis R D; Roth H R; Rosenfeld M J; Smith E C; Wright J J; Buchanan J O; Brassard C L; Gamberdella M; Gillespie E; +. (Department of Chemistry, Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, Connecticut 06492.) Journal of medicinal chemistry, (1992 Jul 10) 35 (14) 2688-96. Journal code: 9716531. ISSN: 0022-2623. Pub. country: United States. Language: English.

AB Two series of 1,3-dihydro-2H-imidazo[4,5-b]quinolin-2-one derivatives incorporating an additional site for acid **salt formation** were synthesized and evaluated as inhibitors of human blood platelet cAMP phosphodiesterase (PDE) and ADP-induced platelet aggregation. The objective of this study was to identify compounds that blended potent biological activity with a satisfactory level of aqueous **solubility**. From a series of 7-aminoimidazo[4,5-b]quinolin-2-ones, biological and physical properties were optimally combined in the 1-piperidinyl derivative 11c. However, this compound offered no significant advantage over earlier studied compounds as an antithrombotic agent in an animal model of small vessel thrombosis. A series of 7-alkoxy alkanoic piperazinamide derivatives, in which the additional basic nitrogen atom was remote from the heterocyclic nucleus and accommodated in a secondary binding region of the cAMP PDE enzyme, demonstrated greater intrinsic cAMP PDE inhibitory activity. Structural modifications of this series focused on variation of the piperazine substituent and side-chain length. The lipophilicity of the N-substituent influenced biological potency and aqueous **solubility**, with substituents of seven carbon atoms or less generally providing acceptable **solubility** properties. The N-(cyclohexylmethyl)piperazinamide 21h was identified from this series of compounds as a potent inhibitor of platelet cAMP PDE, IC50 = 0.4 nM, and ADP-induced platelet aggregation, IC50 = 0.51 microM after a 3-min exposure and 0.1 microM after a 15-min exposure of platelet-rich plasma to the drug. Evaluation of 21h and representative analogues in vivo using a rabbit model of small vessel thrombosis revealed significantly greater antithrombotic efficacy compared to that of previously studied compounds with similar intrinsic biological activity measured in vitro but inferior aqueous **solubility**.

h eb c g cg b cg eb

L3 ANSWER 17 OF 458 MEDLINE on STN

Show References

87195190. PubMed ID: 3571371. Diffusion coefficients of proteins in carrier ampholyte versus immobiline gels. Gelfi C; Bossi M L; Righetti P G. Journal of chromatography, (1987 Mar 18) 390 (1) 225-36. Journal code: 0427043. ISSN: 0021-9673. Pub. country: Netherlands. Language: English.

AB The apparent diffusion coefficients of proteins in carrier ampholyte isoelectric focusing (CA-IEF) and in immobilized pH gradients (IPGs) are strongly dependent on the amount of buffering ions present in the system. However, whereas in CA-IEF increased levels of ampholytes facilitate diffusion, in IPGs they strongly quench it. It is concluded that a protein in an IPG matrix is isoelectric but not isoionic, in the sense that it forms a salt with the surrounding ions bound to the polyacrylamide matrix. This **salt formation** is beneficial as it greatly increases protein **solubility** at the pI. It is suggested that, when performing zymograms in situ, the IPG gel should contain at least twice the standard amount of Immobiline, so as to keep sharp enzyme bands even with prolonged incubation periods.

L3 ANSWER 18 OF 458 MEDLINE on STN

Show References

86253566. PubMed ID: 3459849. Increasing **solubility** of enoxacin and norfloxacin by means of **salt formation**. Spurlock C H. Journal of parenteral science and technology : a publication of the Parenteral Drug Association, (1986 Mar-Apr) 40 (2) 70-2. Journal code: 8103145. ISSN: 0279-7976. Pub. country: United States. Language: English.

L3 ANSWER 19 OF 458 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

Show References

2004:393661 Document No.: PREV200400390650. Modification of physicochemical and mechanical properties of shellac by partial hydrolysis. Limmatvapirat, Sontaya; Limmatvapirat, Chutima; Luangtana-Anan, Manee; Nunthanid, Jurairat; Oguchi, Toshio; Tozuka, Yuichi; Yamamoto, Keiji; Puttipipatkhachorn, Satit [Reprint Author]. Fac PharmDept Mfg Pharm, Mahidol Univ, 447 Sri Ayundhya Rd, Bangkok, 10400, Thailand. pyspt@mucc.maludol.ac.th. International Journal of Pharmaceutics (Kidlington), (June 18 2004) Vol. 278, No. 1, pp. 41-49. print. ISSN: 0378-5173 (ISSN print). Language: English.

AB The shellac was modified by partial hydrolysis with 2.0% (w/w) NaOH for different times. The hydrolysed shellac was then evaluated for physicochemical and film properties in comparison with native shellac. The tablets coated with native and hydrolysed shellac were also evaluated. The results demonstrated that acid value (AV) of shellac increased with prolongation of hydrolysis time. The **solubility** of shellac in buffer solution (pH ltoreq 7) gradually increased with increasing hydrolysis time. The films prepared from hydrolysed shellac were more flexible and soft than those prepared from native shellac. The increasing of flexibility was correlated with the increasing of soft resin in shellac. The water vapor permeability of hydrolysed shellac film was lower than that of native shellac film. The higher acid permeability of the tablet coated with hydrolysed shellac was observed. In ethanol-based film coating, shellac had lower **solubility** and thus lower drug dissolution from coated tablets was observed. In ammonia-based film coating, the **solubility** of shellac was improved higher nearby pH 7.0 by an ammonium neutralisation method because of forming well-soluble salts, thereby higher drug dissolution was obtained. Partial hydrolysis provided

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modified shellac, which is more effective for ammonium **salt formation**, thus very higher drug dissolution was achieved in the ammonia-based coated tablets.

L3 ANSWER 20 OF 458 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on

STN

2003:442384 Document No.: PREV200300442384. Design and synthesis of poly(ADP-ribose)polymerase-1 (PARP-1) inhibitors. Part 3: In vitro evaluation of 1,3,4,5-tetrahydro-benzo(c)(1,6)- and (c)(1,7)-naphthyridin-6-ones. Ferraris, Dana [Reprint Author]; Ficco, Rica Pargas; Pahutski, Thomas; Lautar, Susan; Huang, Shirley; Zhang, Jie; Kalish, Vincent. Guilford Pharmaceuticals Inc., 6611 Tributary Street, Baltimore, MA, 21224, USA. ferrarisd@guilfordpharm.com. Bioorganic & Medicinal Chemistry Letters, (4 August 2003) Vol. 13, No. 15, pp. 2513-2518. print.
CODEN: BMCLE8. ISSN: 0960-894X. Language: English.

AB The 1,3,4,5-tetrahydro-benzo(c)(1,6)- and (c)(1,7)-napthyridin-6-ones are presented as a potent class of PARP-1 inhibitors. Derivatives of these partially saturated aza-5(H)-phenanthridin-6-ones were designed and synthesized with tertiary amines for **salt formation**, thus enhancing aqueous **solubility**, iv formulation and their potential use in acute ischemic injuries (i.e., myocardial ischemia and stroke). We found that partial saturation of the C-ring results in derivatives that are several times more potent than the aromatic C-ring derivatives. The general synthetic routes are presented herein as well as thorough in vitro potencies and SAR discussion for selected derivatives.

L3 ANSWER 21 OF 458 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on

STN

2003:210261 Document No.: PREV200300210261. Effect of buffer media composition on the **solubility** and effective permeability coefficient of ibuprofen. Levis, Karl A.; Lane, Majella E.; Corrigan, Owen I. [Reprint Author]. Department of Pharmaceutics and Pharmaceutical Technology, School of Pharmacy, Trinity College Dublin, Dublin 2, Ireland. ocorrign@tcd.ie. International Journal of Pharmaceutics (Kidlington), (6 March 2003) Vol. 253, No. 1-2, pp. 49-59. print.
ISSN: 0378-5173 (ISSN print). Language: English.

AB The effect of perfusion medium composition on the two important biopharmaceutical parameters drug **solubility** and permeability was determined for ibuprofen. Eight commonly used buffers were examined. Equilibrium **solubility**, buffer capacity profiles and permeability coefficients, using the in situ rat gut perfusion model, were determined for each medium at 37degreeC. The **solubility** of ibuprofen differed sixfold over the range of buffer systems studied. The differences in **solubility** were associated with different pHs of the buffers when saturated with drug and also the presence of micelles and divalent ions. The **solubility** of ibuprofen in FeSSIF was significantly higher than predicted from the pH due to micellisation, while that in Krebs was significantly lower due to ibuprofen-calcium **salt formation**. Buffer capacities varied over a 40-fold range. The pKa values of the buffer components were determined from the buffer capacity versus pH profiles and were in good agreement with the thermodynamic values when corrected for temperature and ionic strength. Smaller, but statistically significant differences in Papp values for ibuprofen were also observed between some of the buffers. During perfusion, pHs of the perfusate samples gradually changed over time towards a median value of approximately 6.5. HBSS gave a Papp apprx50% greater than that observed in PBS 7.4. Physicochemical

factors such as medium pH, buffer capacity and osmolarity should be considered when determining the Papp values of ionisable compounds. Care needs to be exercised when comparing Papp values from different laboratories as buffer composition can have a significant effect on both **solubility** and permeability of a drug, whose ionisation is substantially changed over the pH range of the buffers. Despite the high amount ionised, ibuprofen appears to be well absorbed and it can be classified as a highly permeable drug.

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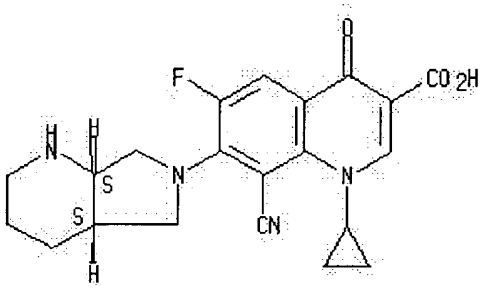

L9 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | +Bibliography and References

ACCESSION NUMBER: 2003:971863 HCAPLUS
DOCUMENT NUMBER: 140:31484
TITLE: Pharmaceutical preparations, especially quinolone antibiotics, for oral administration, containing ion-exchange resins loaded with active ingredients and intrinsically viscous gelling agents as thickening agents
INVENTOR(S): Mertin, Dirk; Edingloh, Markus; Daube, Gert
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003101422	A2	20031211	WO 2003-EP5228	20030519
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10224086	A1	20031211	DE 2002-10224086	20020531

PRIORITY APPLN. INFO.: DE 2002-10224086 A 20020531

AB The invention relates to pharmaceutical prepns. for oral administration, said prepns. contg. at least one active ingredient which is bound to an ion exchanger. The inventive prepns. also contain an intrinsically viscous gelling agent as a thickening agent in order to improve their phys. stability and acceptance, esp. by animals. Thus 0.18 kg methyl-p-hydroxybenzoate and 0.02 kg propyl-p-hydroxybenzoate were dissolved in 75.0 kg hot water; 0.3 kg Xanthan gum and 0.3 kg bentonite were added under vigorous mixing; mixing was continued for one hour at 70°C. The mixt. was cooled; 6.0 kg pradofloxacin, 18.0 kG Amberlite IRP 64 and 1.0 kg vanillin were added to the sol.

IT **195532-12-8**, Pradofloxacin
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pharmaceutical prepns., esp. quinolone antibiotics, for oral

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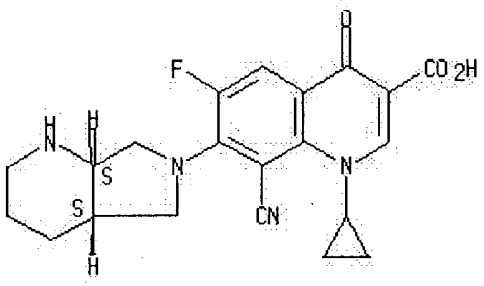
administration, contg. ion-exchange resins loaded with active ingredients and intrinsically viscous gelling agents as thickening agents)

RN 195532-12-8 HCAPLUS

CN 3-Quinolinecarboxylic acid, 8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-7-[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:744337 HCAPLUS

DOCUMENT NUMBER: 139:301379

TITLE: Clinical efficacy and safety of pradofloxacin in the treatment of canine pyoderma and wound infections under field conditions

AUTHOR(S): Stephan, B.; Hellmann, K.; Liege, P.; Granier, S.; Knoppe, T. N.; Heinen, E.; Greife, H. A.

CORPORATE SOURCE: Animal Health Business Group, Bayer AG, Leverkusen, Germany

SOURCE: Journal of Veterinary Pharmacology and Therapeutics (2003), 26(Suppl. 1), 217-218
CODEN: JVPTD9; ISSN: 0140-7783

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Pradofloxacin is a novel 8-cyanofluoroquinolone with improved in vitro activity against a wide range of pathogenic bacteria. Tablets of different strengths are currently developed for the treatment of bacterial infections in dogs and cats. The objective of this work was to assess the clin. efficacy and safety of pradofloxacin in the treatment of canine pyoderma and wound infections.

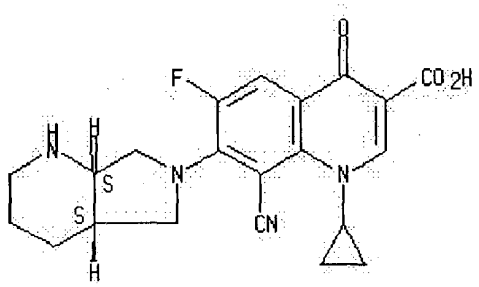
IT **195532-12-8**, Pradofloxacin

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clin. efficacy and safety of pradofloxacin in treatment of canine pyoderma and wound infections under field conditions)

RN 195532-12-8 HCAPLUS

CN 3-Quinolinecarboxylic acid, 8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-7-[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

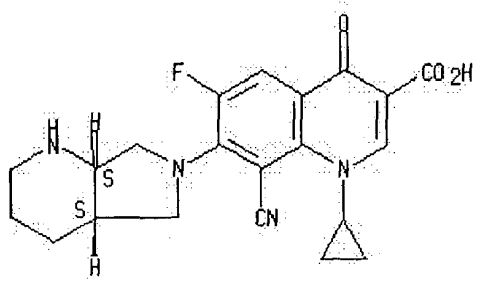
ACCESSION NUMBER: 2003:744304 HCAPLUS
DOCUMENT NUMBER: 140:331682
TITLE: Analytical method for the determination of pradofloxacin in serum and urine by turbulent flow chromatography/tandem mass spectrometry
AUTHOR(S): Krebber, R.
CORPORATE SOURCE: Bayer CropScience AG, BCS-D-ROCS, Monheim, Germany
SOURCE: Journal of Veterinary Pharmacology and Therapeutics (2003), 26(Suppl. 1), 102-103
CODEN: JVPTD9; ISSN: 0140-7783
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A high-throughput anal. method was developed and validated for the detn. of pradofloxacin (PRA) concns. in body fluids. A turbulent flow chromatog. system 2300 HTLC with auto injector CTC HTS PAL coupled to a tandem mass spectrometer Sciex API 365 was used. Serum and urine samples of dogs and cats were analyzed within a mean accuracy between -1 and 4% and a precision between 5.1 and 7.8%. The method enables direct anal. of PRA in several body fluids. It combines a min. of sample prepn. with fast and highly selective detn. within an extremely wide range of linearity and is therefore highly suitable to assess PRA concns. in pharmacokinetic studies.

IT **195532-12-8**, Pradofloxacin
RL: ANT (Analyte); ANST (Analytical study)
(anal. method for detn. of pradofloxacin in serum and urine by turbulent flow chromatog./tandem mass spectrometry in cats and dogs)

RN 195532-12-8 HCAPLUS
CN 3-Quinolinecarboxylic acid, 8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-7-[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

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RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

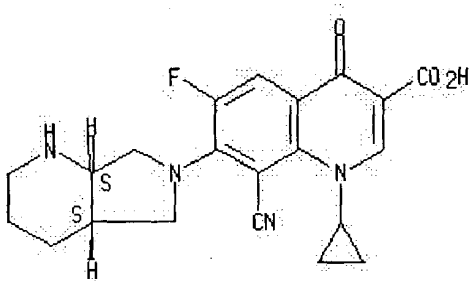
ACCESSION NUMBER: 2003:744303 HCAPLUS
DOCUMENT NUMBER: 140:331734
TITLE: Protein binding of pradofloxacin, a novel 8-cyanofluoroquinolone, in dog and cat plasma
AUTHOR(S): Bregante, M. A.; De Jong, A.; Calvo, A.; Hernandez, E.; Rey, R.; Garcia, M. A.
CORPORATE SOURCE: Veterinary Faculty of University of Zaragoza, Zaragoza, Spain
SOURCE: Journal of Veterinary Pharmacology and Therapeutics (2003), 26(Suppl. 1), 87-88
CODEN: JVPTD9; ISSN: 0140-7783
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The in vitro protein binding of pradofloxacin (PRA) in plasma of dogs and cats was investigated. Enrofloxacin (ENR), the first veterinary fluoroquinolone, was tested as a ref. drug. For concns. of 0.15, 0.75 and 1.50 μg/mL, the percentages of free unbound drug in dog plasma were 63.4±14.8, 63.6±10.5 and 64.2±8.8 for PRA and 59.7±13.3, 54.3±7.3 and 68.4±5.0 for ENR, resp. In cat plasma, the percentages unbound drug were 68.6±7.8, 70.4±11.5, and 71.2±6.2 for PRA and 63.7±10.5, 66.0±9.8 and 73.4±12.5 for ENR. The plasma protein binding of PRA amounted to 29-37% over a ten-fold concn. range: similar findings for ENR (27-46% bound) are in agreement with previous results. A concn. dependency was absent for PRA, but in case of ENR there were statistically significant differences both in dogs and cats; the numerical differences, however, were small.

IT **195532-12-8**, Pradofloxacin
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein binding of pradofloxacin, novel 8-cyanofluoroquinolone, in dog and cat plasma)

RN 195532-12-8 HCAPLUS
CN 3-Quinolinecarboxylic acid, 8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-7-[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

h eb c g cg b cg eb

ACCESSION NUMBER: 2003:76654 HCAPLUS
DOCUMENT NUMBER: 138:126984
TITLE: Pharmaceutical preparations for oral administration containing ion exchange resins loaded with active ingredients
INVENTOR(S): Mertin, Dirk; Block, Wolfgang; Hamann, Hans-juergen
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003007995	A2	20030130	WO 2002-EP7417	20020704
WO 2003007995	A3	20030731		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10134719	A1	20030206	DE 2001-10134719	20010717
EP 1411894	A2	20040428	EP 2002-743262	20020704
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002011149	A	20040629	BR 2002-11149	20020704
PRIORITY APPLN. INFO.:			DE 2001-10134719 A	20010717
			WO 2002-EP7417 W	20020704

AB The invention relates to pharmaceutical prepns. contg. at least one active ingredient which is linked to an ion exchanger. In order to improve the palatability and to increase the stability, at least 90 % of said active ingredient/ion exchanger particles are smaller than 50 μm. Quinolone antibiotics are bound to cation exchange resins, esp. for the prepn. cat medication. Thus 3.86 kg enrofloxacin and 19.24 kg Amberlite IRP64 were suspended in 76.90 kg purified water and stirred for at least 8 h at room temp. The suspension was transferred to a filter dryer, filtered and dryed at 85°C. The obtained 17.96 kg of enrofloxacin-loaded resin was suspended with 60 g colloidal silica, 100.30 kg neutral oil (e.g. Miglyol 812) and ground in a perl mill; at least 90% of the particles were smaller than 10 μm.

IT **195532-12-8**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical prepns. for oral administration contg. ion exchange resins loaded with active ingredients)
RN 195532-12-8 HCAPLUS
CN 3-Quinolinecarboxylic acid, 8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-7-[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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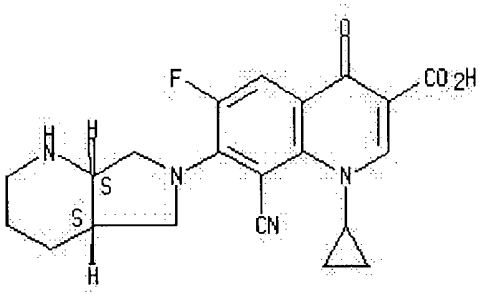


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L9             6 S L7 NOT L8
L10            0 S L9 AND RAST, H?/AU

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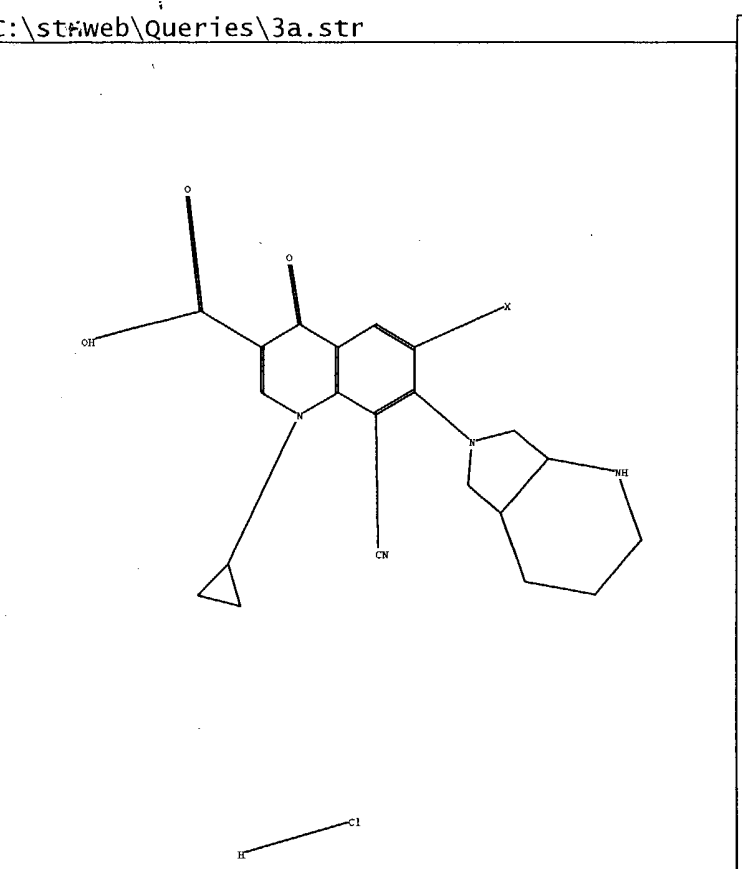

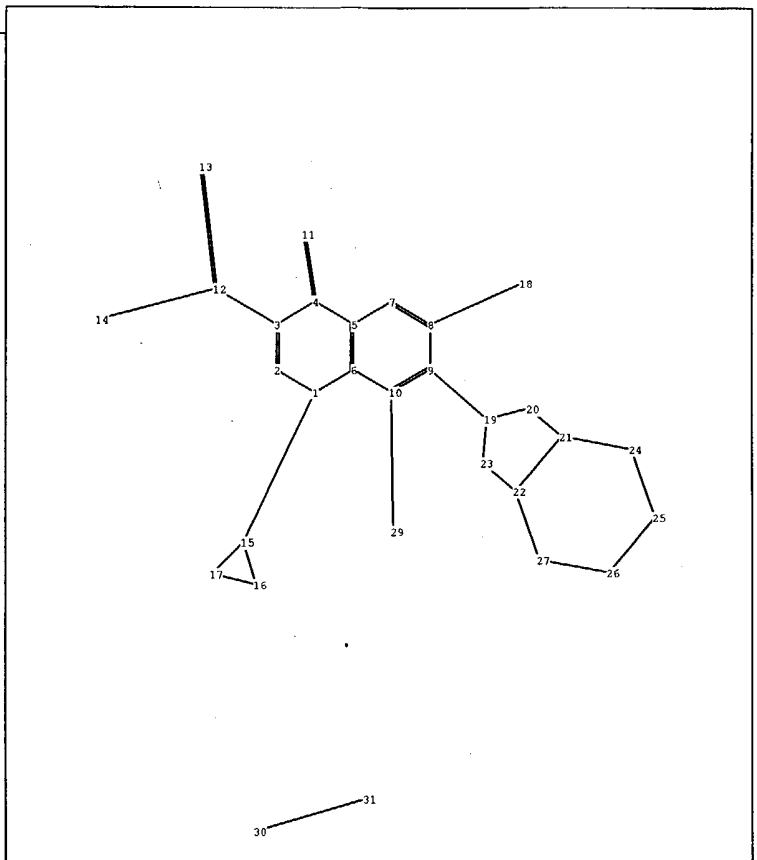

chain nodes :
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ring nodes :
1 2 3 4 5 6 7 8 9 10 15 16 17 19 20 21 22 23 24 25 26 27
chain bonds :
1-15 3-12 4-11 8-18 9-19 10-29 12-13 12-14 30-31
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 15-16 15-17 16-17 19-20
19-23 20-21 21-22 21-24 22-23 22-27 24-25 25-26 26-27
exact/norm bonds :
1-2 1-6 1-15 2-3 3-4 4-5 4-11 9-19 15-16 15-17 16-17 19-20 19-23 21-22
21-24 22-27 24-25 25-26 26-27
exact bonds :
3-12 8-18 10-29 20-21 22-23 30-31
normalized bonds :
5-6 5-7 6-10 7-8 8-9 9-10 12-13 12-14
Isolated ring systems :
containing 1 : 19 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:CLASS
12:CLASS 13:CLASS 14:CLASS 15:Atom 16:Atom 17:Atom 18:CLASS 19:Atom 20:Atom
21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 29:CLASS 30:CLASS
31:CLASS

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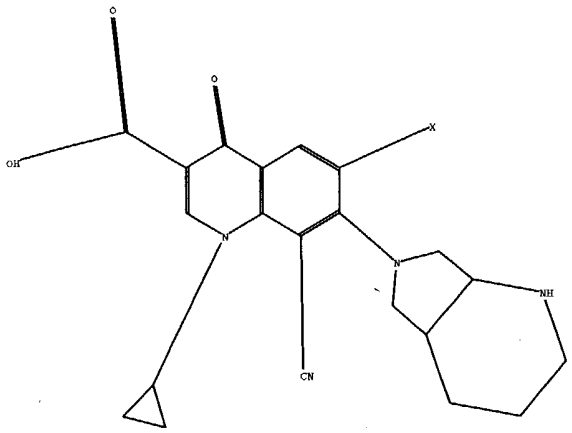

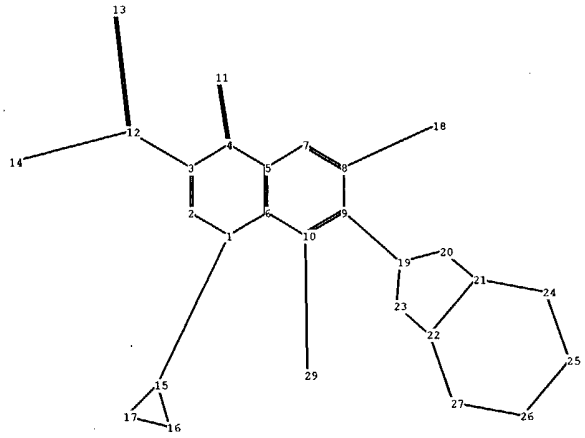

chain nodes :
11 12 13 14 18 29
ring nodes :
1 2 3 4 5 6 7 8 9 10 15 16 17 19 20 21 22 23 24 25 26 27
chain bonds :
1-15 3-12 4-11 8-18 9-19 10-29 12-13 12-14
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 15-16 15-17 16-17 19-20
19-23 20-21 21-22 21-24 22-23 22-27 24-25 25-26 26-27
exact/norm bonds :
1-2 1-6 1-15 2-3 3-4 4-5 4-11 9-19 15-16 15-17 16-17 19-20 19-23 21-22
21-24 22-27 24-25 25-26 26-27
exact bonds :
3-12 8-18 10-29 20-21 22-23
normalized bonds :
5-6 5-7 6-10 7-8 8-9 9-10 12-13 12-14
isolated ring systems :
containing 1 : 19 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:CLASS
12:CLASS 13:CLASS 14:CLASS 15:Atom 16:Atom 17:Atom 18:CLASS 19:Atom 20:Atom
21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 29:CLASS

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* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1            Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2            "Ask CAS" for self-help around the clock
 NEWS  3  SEP 01    INPADOC: New family current-awareness alert (SDI) available
 NEWS  4  SEP 01    New pricing for the Save Answers for SciFinder Wizard within
                    STN Express with Discover!
 NEWS  5  SEP 01    New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
 NEWS  6  SEP 27    STANDARDS will no longer be available on STN
 NEWS  7  SEP 27    SWETSCAN will no longer be available on STN
 NEWS  8  OCT 28    KOREAPAT now available on STN
 NEWS  9  NOV 18    Current-awareness alerts, saved answer sets, and current
                    search transcripts to be affected by CERAB, COMPUAB, ELCOM,
                    and SOLIDSTATE reloads

 NEWS EXPRESS  OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
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FILE 'HOME' ENTERED AT 19:16:30 ON 24 NOV 2004

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'REGISTRY' ENTERED AT 19:16:39 ON 24 NOV 2004
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STRUCTURE FILE UPDATES:   23 NOV 2004  HIGHEST RN 787526-19-6
DICTIONARY FILE UPDATES:  23 NOV 2004  HIGHEST RN 787526-19-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.
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h eb c g cg b cg eb

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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L1 STRUCTURE UPLOADED

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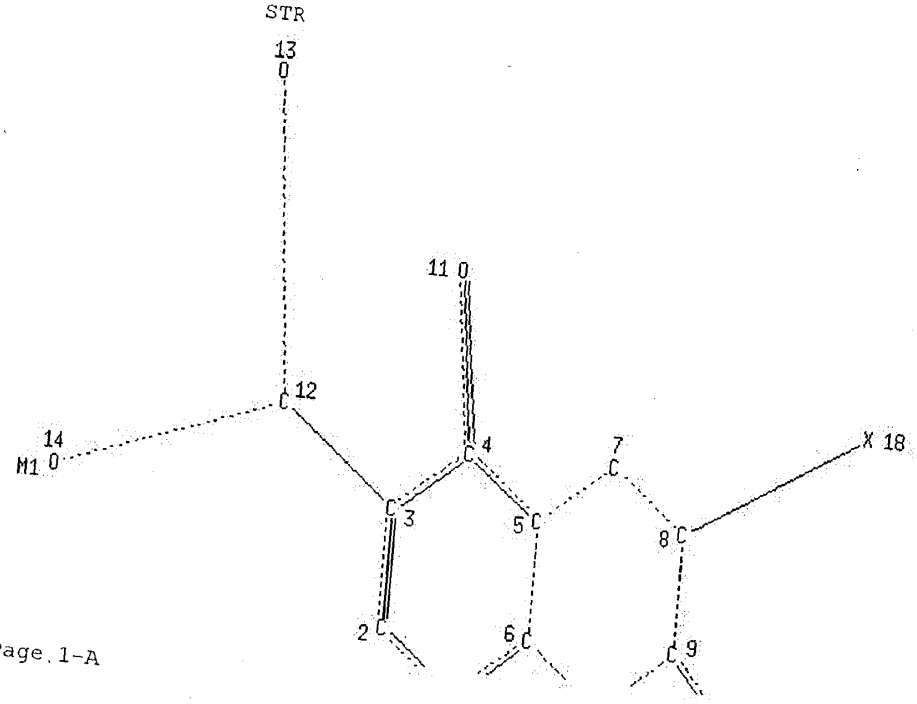
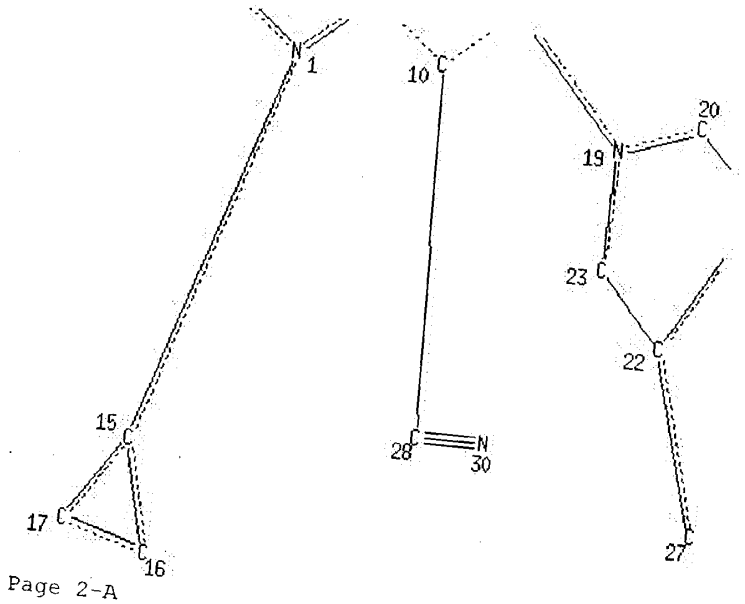
L1 HAS NO ANSWERS
L1 STR



Page 1-A



Page 2-A

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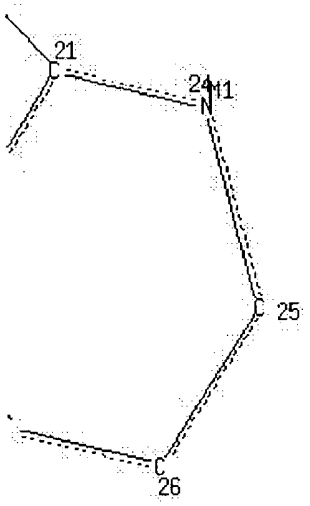

Page 2-B

29 Cl M1

Page 3-A

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HCOUNT	IS M1	AT	29
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NSPEC	IS R	AT	6
NSPEC	IS R	AT	7
NSPEC	IS R	AT	8
NSPEC	IS R	AT	9
NSPEC	IS R	AT	10
NSPEC	IS C	AT	11
NSPEC	IS C	AT	12
NSPEC	IS C	AT	13
NSPEC	IS C	AT	14
NSPEC	IS R	AT	15
NSPEC	IS R	AT	16
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NSPEC	IS R	AT	19
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NSPEC	IS R	AT	27
NSPEC	IS C	AT	28
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NSPEC	IS C	AT	30

DEFAULT MLEVEL IS ATOM

MLEVEL IS CLASS AT 11 12 13 14 18 28 29 30

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

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RSPEC   1  19
NUMBER OF NODES IS  30

STEREO ATTRIBUTES: NONE


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SAMPLE SCREEN SEARCH COMPLETED -     81 TO ITERATE

100.0% PROCESSED      81 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         1081 TO     2159
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
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FULL SCREEN SEARCH COMPLETED -   1885 TO ITERATE

100.0% PROCESSED    1885 ITERATIONS                               0 ANSWERS
SEARCH TIME: 00.00.01

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=>
L4      STRUCTURE UPLOADED

=> s l4
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SAMPLE SCREEN SEARCH COMPLETED -     81 TO ITERATE

100.0% PROCESSED      81 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

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                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         1081 TO     2159
PROJECTED ANSWERS:               0 TO        0

L5            0 SEA SSS SAM L4

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FULL SCREEN SEARCH COMPLETED -   1885 TO ITERATE

100.0% PROCESSED    1885 ITERATIONS                               7 ANSWERS
SEARCH TIME: 00.00.01

L6            7 SEA SSS FUL L4

=> file hcaplus
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h eb c g cg b cg eb

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	313.36	313.57

FILE 'HCAPLUS' ENTERED AT 19:21:40 ON 24 NOV 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 24 Nov 2004 VOL 141 ISS 22
FILE LAST UPDATED: 23 Nov 2004 (20041123/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L7          12 L6

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            61 HIMMLER, T?/AU
L8           6 L7 AND HIMMLER, T?/AU

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L8 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:607382 HCAPLUS
DOCUMENT NUMBER: 133:213147
TITLE: Crystal modification C of 8-cyano-1-cyclopropyl-7-[(1S,6S)-2,8-diazabicyclo[4.3.0]nonan-8-yl]-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid
INVENTOR(S): Rast, Hubert; **Himmler, Thomas**
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Ger. Offen., 12 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19908449	A1	20000831	DE 1999-19908449	19990226
CA 2362801	AA	20000908	CA 2000-2362801	20000214
WO 2000052009	A1	20000908	WO 2000-EP1202	20000214

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h eb c g cg b cg eb

IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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TR 200102434	T2	20020321	TR 2001-200102434	20000214
JP 2002538158	T2	20021112	JP 2000-602235	20000214
AT 226952	E	20021115	AT 2000-909166	20000214
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NO 2001004061	A	20010821	NO 2001-4061	20010821
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			WO 2000-EP1202 W	20000214

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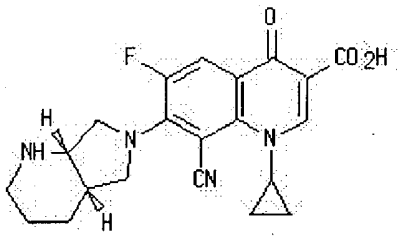


I

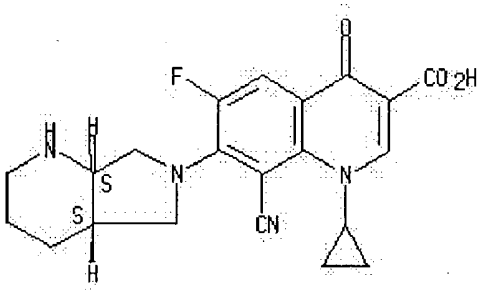
AB The title compd. (I) is converted to stable crystal modification C (m. 235-237°) by holding I at room temp. and relative humidity ≥92% until no further wt. gain occurs, drying, and heating to above the conversion temp. (150-180°). I modification D is characterized by its powder x-ray diffractogram, IR spectrum, and by DTA. I is highly active against pathogenic bacteria in human and veterinary medicine.

IT **195532-12-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(crystal modification D of cyanocyclopropyl(diazabicyclononanyl)fluorodihydrooxoquinolinecarboxylic acid)

RN 195532-12-8 HCAPLUS

CN 3-Quinolinecarboxylic acid, 8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-7-[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:607381 HCAPLUS
DOCUMENT NUMBER: 133:213146
TITLE: Crystal modification D of 8-cyano-1-cyclopropyl-7-[(1S,6S)-2,8-diazabicyclo[4.3.0]nonan-8-yl]-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid
INVENTOR(S): **Himmler, Thomas**; Rast, Hubert
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Ger. Offen., 12 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19908448	A1	20000831	DE 1999-19908448	19990226
CA 2362804	AA	20000908	CA 2000-2362804	20000214
WO 2000052010	A1	20000908	WO 2000-EP1203	20000214
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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NO 2001004059	A	20010821	NO 2001-4059	20010821
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PRIORITY APPLN. INFO.:

DE 1999-19908448	A	19990226
WO 2000-EP1203	W	20000214

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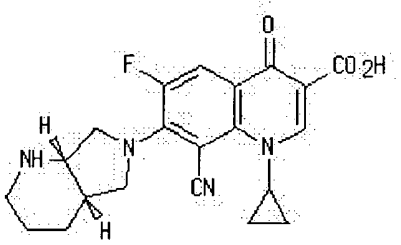


I

AB The title compd. (I) is converted to stable crystal modification D (m. 261-265°) by dissolving I in H2O to a concn. of 1-3 wt.%, allowing the soln. to stand until a ppt. forms, removing the ppt. by filtration, drying the remaining soln., and heating the solid obtained to above the transition temp. (130-160°). I modification D is characterized by its powder x-ray diffractogram, IR spectrum, and by DTA. I is highly active against pathogenic bacteria in human and veterinary medicine.

IT **195532-12-8**

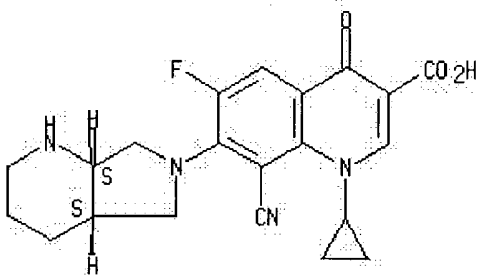
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(crystal modification D of cyanocyclopropyl(diazabicyclononanyl)fluorodihydrooxoquinolinecarboxylic acid)

RN 195532-12-8 HCAPLUS

CN 3-Quinolinecarboxylic acid, 8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-7-[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Refs

ACCESSION NUMBER: 2000:366037 HCAPLUS
DOCUMENT NUMBER: 133:4647
TITLE: Semihydrochloride of 8-cyano-1-cyclopropyl-7-(1S,6S-2,8-diazabicyclo[4.3.0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid
INVENTOR(S): **Himmler, Thomas**; Rast, Hubert
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Ger. Offen., 16 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19854357	A1	20000531	DE 1998-19854357	19981125

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RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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AT 225790		E	20021015	AT 1999-955995	19991115
ES 2181488		T3	20030216	ES 1999-955995	19991115
PT 1133495		T	20030228	PT 1999-955995	19991115
AU 759769		B2	20030501	AU 2000-12716	19991115
NZ 511863		A	20030530	NZ 1999-511863	19991115
NO 2001002532		A	20010702	NO 2001-2532	20010523
PRIORITY APPLN. INFO.:				DE 1998-19854357	A 19981125
				WO 1999-EP8778	W 19991115

OTHER SOURCE(S): CASREACT 133:4647

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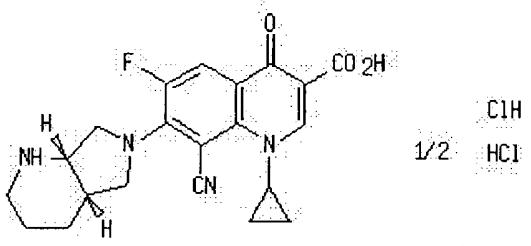


I

AB The title compd. (I), useful as a medical and veterinary bactericide, shows good water soly. (19 wt.%). I is produced by reaction of 7-halo-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid with (1S,6S)-2,8-diazabicyclo[4.3.0]nonane in the presence of a base in one of the following diluents: (a) a C≥4 aliph. alc., (b) a mixt. of a C>3 alc. with the polar aprotic diluent, N-methylpyrrolidone; (c) a mixt. of n-PrOH with DMF. I (m. 278-280°) is characterized by its powder x-ray diffractogram, differential thermogram, and IR spectrum.

IT **271252-05-2P**

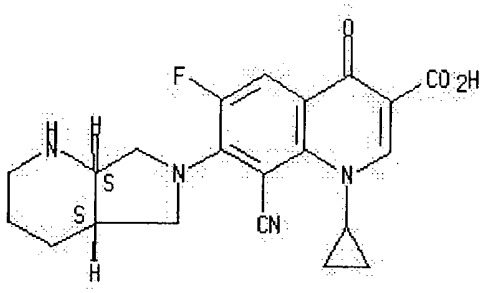
RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(semihydrochloride of cyanocyclopropyl(diazabicyclononyl)fluorodihydrooxoquinolinecarboxylic acid)

RN 271252-05-2 HCAPLUS

CN 3-Quinolinecarboxylic acid, 8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-7-[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4-oxo-, hydrochloride (2:1) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

h eb c g cg b cg eb



1/2 HCl

L8 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

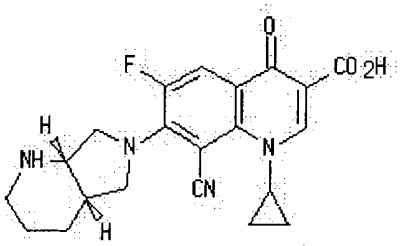
ACCESSION NUMBER: 2000:366036 HCAPLUS
DOCUMENT NUMBER: 133:4646
TITLE: Crystal modification A of 8-cyano-1-cyclopropyl-7-(1S,6S-2,8-diazabicyclo[4.3.0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid
INVENTOR(S): **Himmler, Thomas**; Hallenbach, Werner; Rast, Hubert
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Ger. Offen., 8 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19854356	A1	20000531	DE 1998-19854356	19981125
CA 2351712	AA	20000602	CA 1999-2351712	19991115
WO 2000031075	A1	20000602	WO 1999-EP8775	19991115
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 9915669	A	20010814	BR 1999-15669	19991115
EP 1133496	A1	20010919	EP 1999-958040	19991115
EP 1133496	B1	20040421		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200101438	T2	20011022	TR 2001-200101438	19991115
JP 2002530406	T2	20020917	JP 2000-583903	19991115
NZ 511861	A	20021220	NZ 1999-511861	19991115
AU 763883	B2	20030731	AU 2000-15533	19991115
CN 1135229	B	20040121	CN 1999-813686	19991115
TW 576835	B	20040221	TW 1999-88119810	19991115
AT 264858	E	20040515	AT 1999-958040	19991115
PT 1133496	T	20040831	PT 1999-958040	19991115
NO 2001002460	A	20010518	NO 2001-2460	20010518
US 6436955	B1	20020820	US 2001-856669	20010523

h eb c g cg b cg eb

PRIORITY APPLN. INFO.: DE 1998-19854356 A 19981125
WO 1999-EP8775 W 19991115

GI



I

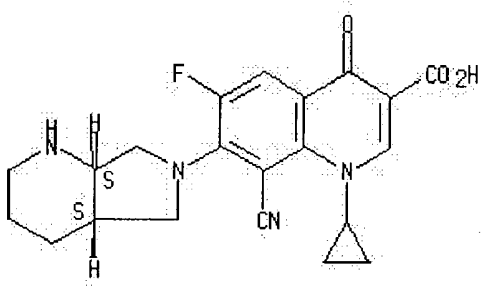
AB The title compd. in crystal modification A (I), useful as a medical and veterinary bactericide, is stable during extended storage without conversion to the amorphous form or any other crystal modification, and is less hygroscopic than the amorphous form of the compd. I is produced by dissolving the amorphous compd. or an unknown modification of it in hot water or a hot water-alc. mixt., adding an alc. (esp. EtOH or iso-PrOH), and cooling to room temp. I (m. 249-252°) is characterized by its powder x-ray diffractogram, differential thermogram, and IR spectrum.

IT **195532-12-8P**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(crystal modification A of cyanocyclopropyl(diazabicyclononyl)fluorodihydrooxoquinolinecarboxylic acid)

RN 195532-12-8 HCAPLUS

CN 3-Quinolinecarboxylic acid, 8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-7-[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:366035 HCAPLUS
DOCUMENT NUMBER: 133:4645
TITLE: Crystal modification B of 8-cyano-1-cyclopropyl-7-(1S,6S-2,8-diazabicyclo[4.3.0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid
INVENTOR(S): **Himmler, Thomas**; Hallenbach, Werner; Rast, Hubert
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Ger. Offen., 8 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1

h eb c g cg b cg eb

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19854355	A1	20000531	DE 1998-19854355	19981125
CA 2351707	AA	20000602	CA 1999-2351707	19991115
WO 2000031076	A1	20000602	WO 1999-EP8776	19991115
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 9915682	A	20010814	BR 1999-15682	19991115
EP 1133497	A1	20010919	EP 1999-959278	19991115
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200101444	T2	20020121	TR 2001-200101444	19991115
JP 2002530407	T2	20020917	JP 2000-583904	19991115
NZ 511862	A	20030829	NZ 1999-511862	19991115
AU 767890	B2	20031127	AU 2000-16517	19991115
NO 2001002461	A	20010518	NO 2001-2461	20010518
US 6664268	B1	20031216	US 2001-856670	20010523
PRIORITY APPLN. INFO.:			DE 1998-19854355 A	19981125
			WO 1999-EP8776 W	19991115

OTHER SOURCE(S): CASREACT 133:4645

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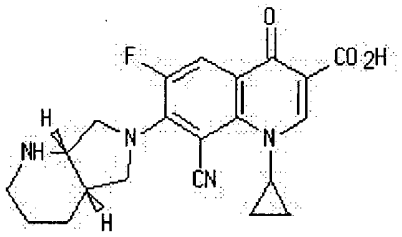


I

AB The title compd. in crystal modification B (I), useful as a medical and veterinary bactericide, is stable during extended storage without conversion to the amorphous form or any other crystal modification, and is less hygroscopic than the amorphous form of the compd. I is produced either (a) by reaction of 7-halo-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid with (1S,6S)-2,8-diazabicyclo[4.3.0]nonane in the presence of a base in a mixt. of EtOH and a polar aprotic diluent such as N-methylpyrrolidone, DMF, or sulfolane, or (b) by heating an unknown modification of the compd. in the presence of a base in EtOH, n-PrOH, iso-PrOH, or a mixt. of one of these alcs. with one of the polar aprotic diluents named previously. I (m. 243-245°) is characterized by its powder x-ray diffractogram, differential thermogram, and IR spectrum.

IT **195532-12-8P**

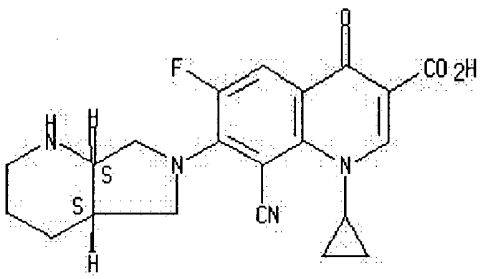
RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(crystal modification B of cyanocyclopropyl(diazabicyclononyl)fluorodihydrooxoquinolinecarboxylic acid)

RN 195532-12-8 HCAPLUS

h eb c g cg b cg eb

CN 3-Quinolinecarboxylic acid, 8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-7-[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 1997:579724 HCAPLUS
DOCUMENT NUMBER: 127:248093
TITLE: 8-Cyano-1-cyclopropyl-7-(2,8-diazabicyclo[4.3.0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid derivatives
INVENTOR(S): Bartel, Stefan; Jaetsch, Thomas; **Himmler, Thomas**; Rast, Hans-Georg; Hallenbach, Werner; Heinen, Ernst; Pirro, Franz; Scheer, Martin; Stegemann, Michael; Stupp, Hans-Peter; Wetzstein, Heinz-Georg
PATENT ASSIGNEE(S): Bayer A.-G., Germany; Bartel, Stefan; Jaetsch, Thomas; Himmler, Thomas; Rast, Hans-Georg; Hallenbach, Werner; Heinen, Ernst; Pirro, Franz; Scheer, Martin; et al.
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9731001	A1	19970828	WO 1997-EP637	19970212
W: AU, BB, BG, BR, BY, CA, CN, CZ, HU, IL, JP, KR, KZ, LK, MX, NO, NZ, PL, RO, RU, SK, TR, UA, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
DE 19633805	A1	19970828	DE 1996-19633805	19960822
ZA 9701507	A	19970916	ZA 1997-1507	19970202
CA 2247020	AA	19970828	CA 1997-2247020	19970212
AU 9717689	A1	19970910	AU 1997-17689	19970212
AU 715341	B2	20000120		
EP 882049	A1	19981209	EP 1997-903260	19970212
EP 882049	B1	20021120		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
CN 1211984	A	19990324	CN 1997-192523	19970212
CN 1073112	B	20011017		
BR 9707606	A	19990727	BR 1997-7606	19970212
NZ 331468	A	20000228	NZ 1997-331468	19970212
JP 2000504734	T2	20000418	JP 1997-529755	19970212
IL 125444	A1	20010319	IL 1997-125444	19970212

h eb c g cg b cg eb

RU 2173318	C2	20010910	RU 1998-117814	19970212
EP 1215202	A1	20020619	EP 2002-6519	19970212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
AT 228130	E	20021215	AT 1997-903260	19970212
CZ 291251	B6	20030115	CZ 1998-2684	19970212
ES 2184060	T3	20030401	ES 1997-903260	19970212
PT 882049	T	20030430	PT 1997-903260	19970212
PL 186737	B1	20040227	PL 1997-328577	19970212
TW 390879	B	20000521	TW 1997-86101994	19970220
US 6323213	B1	20011127	US 1998-125191	19980813
NO 9803819	A	19980820	NO 1998-3819	19980820
HK 1018903	A1	20020510	HK 1999-104030	19990917
US 6278013	B1	20010821	US 2000-718062	20001121
CN 1335301	A	20020213	CN 2001-110855	20010228
PRIORITY APPLN. INFO.:			DE 1996-19606762 A	19960223
			DE 1996-19633805 A	19960822
			EP 1997-903260 A3	19970212
			WO 1997-EP637 W	19970212
			US 1998-125191 A3	19980813

OTHER SOURCE(S): MARPAT 127:248093

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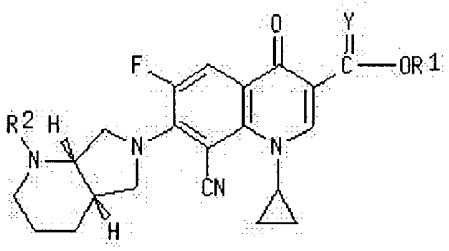


I

AB Title compds. I [R1 = H, alkyl, optionally substituted by OH, OMe, NH2, NHMe, NMe2, or (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl; R2 = H, benzyl, alkyl, (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl, CH=CHCO2R3, CH2CH2CO2R3, CH2CH2CN, CH2CH2COMe, CH2COMe; R3 = Me, Et, R4(NHCHR5CO)n; R4 = H, alkyl, CO2CMe3; R5 = H, alkyl, hydroxyalkyl, aminoalkyl, thioalkyl, carboxyalkyl, benzyl; n = 1, 2; Y = O, S] were prepd. for use as antibacterial agents. Thus, I [R1 = OH, R2 = H, Y = O] was prepd. by aminating the 7-chloroquinoline. I [R1 = OH, R2 = H, Y = O] had min. inhibitory concns. against a no. of bacteria that were superior to those of enrofloxacin.

IT **195532-12-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

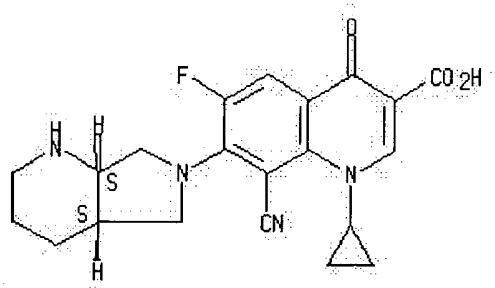
(prepn. of diazabicylononylquinolinecarboxylic acid derivs. as bactericides)

RN 195532-12-8 HCAPLUS

CN 3-Quinolinecarboxylic acid, 8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-7-[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

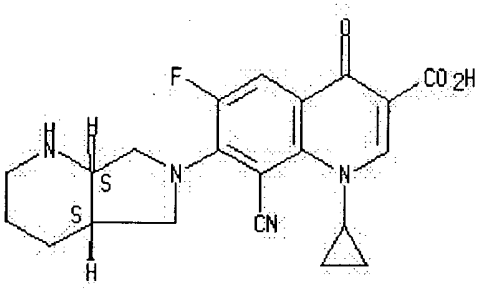
h eb c g cg b cg eb



IT **195532-14-0P 195532-16-2P 195532-18-4P**
195532-20-8P 195532-58-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of diazabicylononylquinolinecarboxylic acid derivs. as bactericides)

RN 195532-14-0 HCAPLUS
CN 3-Quinolinecarboxylic acid, 8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-7-(octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl)-4-oxo-, monohydrochloride, (4aS-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



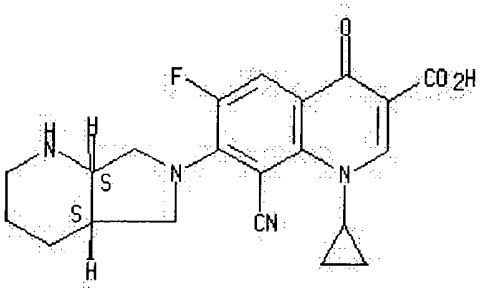
\# HCl

RN 195532-16-2 HCAPLUS
CN 3-Quinolinecarboxylic acid, 8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-7-(octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl)-4-oxo-, (4aS-cis)-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 195532-12-8
CMF C21 H21 F N4 O3

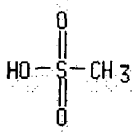
Absolute stereochemistry.



CM 2

h eb c g cg b cg eb

CRN 75-75-2
CMF C H4 O3 S

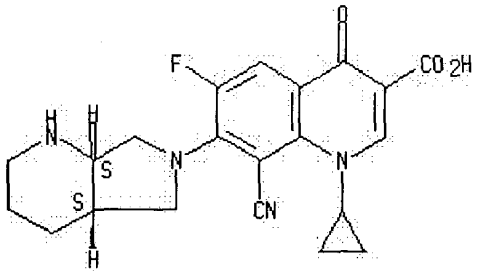


RN 195532-18-4 HCAPLUS
CN 3-Quinolinecarboxylic acid, 8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-7-(octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl)-4-oxo-, (4aS-cis)-, mono(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

CM 1

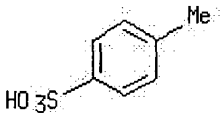
CRN 195532-12-8
CMF C21 H21 F N4 O3

Absolute stereochemistry.



CM 2

CRN 104-15-4
CMF C7 H8 O3 S



RN 195532-20-8 HCAPLUS
CN 3-Quinolinecarboxylic acid, 8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-7-(octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl)-4-oxo-, (4aS-cis)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 195532-12-8
CMF C21 H21 F N4 O3

Absolute stereochemistry.

h eb c g cg b cg eb

=> d ibib abs l22 1-36

L22 ANSWER 1 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:799437 HCAPLUS
DOCUMENT NUMBER: 141:314353
TITLE: Compositions comprising multiple antibiotic agents including a FabI inhibitor, methods of using the same, and preparation of the heterocycle FabI inhibitors
INVENTOR(S): Berman, Judd M.; Schmid, Molly B.; Mendlein, John D.; Kaplan, Nachum
PATENT ASSIGNEE(S): Affinium Pharmaceuticals, Inc., Can.
SOURCE: PCT Int. Appl., 311 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004082586	A2	20040930	WO 2004-IB1261	20040317

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 2003-455189P P 20030317
US 2003-476970P P 20030609
US 2003-488379P P 20030718

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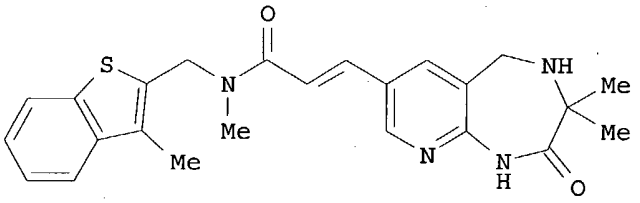

I

AB The invention is directed to antibacterial compns. comprising an NADH (or NADPH)-dependent enoyl-acyl carrier protein (ACP) reductase (FabI, previously designated EnvM) inhibitor of formula (Y1)a-A-CH(R1)-NR1CO-L-R2 (I) and at least one other antibiotic/antibacterial agent [L = alkyl, alkenyl, or cycloalkyl which may be substituted by one or **more** R1; A = (un)substituted bicyclic heteroaryl of 8-12 atoms or a tricyclic ring of 12-16 atoms, containing 1-4 heteroatoms selected from N, S, and O; R1 = cyclo/alkyl, alk/aryl; R2 = heterocyclyl; a = 0-4; Y1 = -(CH2)n-CO-NR4R5; R4 = water **solubilizing** group; R5 = H, cyclo/alkyl; n = 0-4]. The antibacterial composition exhibits a synergistic

antibacterial effect compared to its individual components. Thus, reacting.7-Bromo-3,3-dimethyl-1,3,4,5-tetrahydropyrido[2,3-e][1,4]diazepin-2-one (preparation given) with N-Methyl-N-[(3-methylbenzo[b]thiophen-2-yl)methyl]acrylamide (preparation given), followed by acidulation gave diazepinone salt II•HCl. Selected I inhibited FabI with a Ki < 1 nM, an MIC (minimal inhibitory concentration) < 0.125 μg/mL, and an IC50 < 10 nM.

L22 ANSWER 2 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:534305 HCAPLUS
DOCUMENT NUMBER: 141:87908
TITLE: Large scale production, isolation and purification human interleukin 21 using plasmid vector pTAP337, transformed Escherichia coli, fed batch fermentation and chromatography
INVENTOR(S): Chang, Chung; Zamost, Bruce L.; Covert, Douglas C.; Liu, Hong Y.; De, Jongh Karen S.; Meyer, Jeffrey D.; Holderman, Susan D.
PATENT ASSIGNEE(S): Zymogenetics, Inc., USA
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004055168	A2	20040701	WO 2003-US39764	20031212

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-433448P P 20021213
US 2002-433452P P 20021213

AB The invention discloses an expression vector (pTAP337) comprising an optimized human interleukin 21-encoding nucleic acid sequence (IL-21, previously designated Zα11 ligand), and its use in transforming Escherichia coli for large scale production of IL-21. The invention relates that plasmid pTAP337 utilizes an IL-21 coding sequence with specific changes in nucleotides in order to optimize codons and mRNA secondary structure for translation in E. coli, and encodes the mature form of IL-21 plus a methionine at the N-terminus (designated IL-21met). The invention also relates that using pTAP337, IL-21 was produced in E. coli to a level of **greater** than 1 g/L in fed batch fermentation The invention also discloses the DNA sequence of the optimized human IL-21met, and the amino acid sequence of the encoded protein. The invention further discloses specific materials and methods used in fed batch fermentation and in isolation and purification of recombinant human IL-21met. In the examples, the invention presented the construction of OmpT deficient E. coli strains transformed with an IL-21 expression vector.

L22 ANSWER 3 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:142605 HCAPLUS

DOCUMENT NUMBER: 140:187389
TITLE: Sincalide formulations
INVENTOR(S): Metcalfe, Edmund C.; Monteferrante, Jo Anna; Newborn, Margaret; Ropiak, Irene; Schramm, Ernst; White, Gregory W.; Zodda, Julius P.
PATENT ASSIGNEE(S): Bracco International B.V., USA
SOURCE: U.S. Pat. Appl. Publ., 37 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004033243	A1	20040219	US 2002-222540	20020816
US 6803046	B2	20041012		
PRIORITY APPLN. INFO.:			US 2002-222540	20020816

AB The invention features sincalide formulations that include an effective amount of sincalide, a bulking agent/tonicity adjuster, a stabilizer, a surfactant, a chelator, and a buffer. The invention also features kits and methods for preparing **improved** sincalide formulations, as well as methods for treating, preventing, and diagnosing gall bladder-related disorders using sincalide formulations.

L22 ANSWER 4 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:761005 HCAPLUS
DOCUMENT NUMBER: 138:57461
TITLE: Surfactant-modified supercritical fluids as dissolving media for polar textile dyes
AUTHOR(S): Lewin-Kretzschmar, Uta; Harting, Peter
CORPORATE SOURCE: Institut fuer Nichtklassische Chemie e.V., Universitaet Leipzig, Leipzig, D-04318, Germany
SOURCE: Chemie Ingenieur Technik (2002), 74(9), 1230-1236
CODEN: CITEAH; ISSN: 0009-286X
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: German

AB To **improve solubility** of polar dyes in supercrit. fluids, 3 different surfactants were examined (Na diisooctylsulfosuccinate (Texin), N-dodecylpyridinium chloride, and dodecyloxethpropylate). The **solubilities** of the dyes Primulin, Lissamine Yellow AE, and Parafuchsine **monohydrochloride** were determined in scCO2 and scC2H6 at 373 K and 45 MPa in the presence of surfactants using water, EtOH, pentanol, or MeOH as solvent modifiers. The dye **solubilities** were also determined in unmodified as well as in Texin-modified scCO2 and scC2H6 by varying temperature (323, 348, and 373 K) and pressure. The **solubilities** of the dyes Doractive Blue WRL, Doramin Light Blue BR 200%, and Domalan Blue BL 150% were determined in scCO2 at 373 K and 45 MPa in the presence of Texin using water and EtOH as solvent modifiers. Results show a drastic enhancement of **solubility** when EtOH was added to an aqueous Texin-modified scCO2 system. The Texin/EtOH system was then applied in dyeing of wool with Lissamin Gelb AE at 373 K and 45 MPa. Dyeing trials were insufficient with respect to fastness and homogeneity.

L22 ANSWER 5 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:489100 HCAPLUS
DOCUMENT NUMBER: 133:108524
TITLE: Acidic bath for bismuth coating on copper for protection of electric printed circuits

INVENTOR(S): Piano, Anthony M.
PATENT ASSIGNEE(S): Fry's Metals, Inc., USA
SOURCE: U.S., 6 pp., Cont.-in-part of U.S. Ser. No. 214,050, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6090493	A	20000718	US 1996-704510	19961226
WO 9525008	A1	19950921	WO 1995-US3574	19950317

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1994-214050 B2 19940317
WO 1995-US3574 W 19950317

AB The Cu surface (especially for elec. printed circuits) is protected by the Bi coating from aqueous acidic bath containing: (a) acid-**solubilized** Bi salt, especially Bi2O3 or BiCl3; (b) an iodide (especially KI, NaI, or HI) for **increased** adhesion and improved appearance of the Bi; (c) optional Cu salt at 250-500 ppm for **increased** coating rate; and (d) optional complexing agent. The Bi salt is preferably **solubilized** in HCl or HBr. The typical starting bath contains Bi2O3 5 g, 37% HCl 50 mL, KI 1.25 g, and water for 1 L. The Cu surface can be coated in the bath at pH <4 and 120-200° F with the B film nominally 1-10 μin. thick. The Bi-coated Cu surface is resistant to tarnishing, shows good solderability, and is suitable for elec.-circuit boards.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 6 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:729001 HCAPLUS
DOCUMENT NUMBER: 130:77272
TITLE: Antigenicity of a water soluble dimethyl dimethoxy biphenylate derivative (DDB-S), a new antihepatitis agent
AUTHOR(S): Han, Hyung-Mee; Kim, Jin Ho; Choi, Kyoung Baek; Kim, Hyung Soo; Chung, Seung Tae; Moon, Jeon-Ok; Lee, Chi-Ho; Kim, Jooil
CORPORATE SOURCE: Immunotoxicology Division, Department Toxicology, National Institute Toxicological Research, Korea Food & Drug Administration, Seoul, 122-704, S. Korea
SOURCE: Journal of Toxicology and Public Health (1998), 14(3), 307-313
CODEN: JTPHFT; ISSN: 1226-8399
PUBLISHER: Korean Society of Toxicology
DOCUMENT TYPE: Journal
LANGUAGE: Korean

AB Di-Me dimethoxy biphenylate (DDB) is an agent used to treat hepatitis. DDB-S, i.e. 2-methylaminoethyl 4,4'-dimethoxy-5,6,5',6-dimethylenedioxybiphenyl-2-carboxylic acid 2'-carboxylate **monohydrochloride**, was synthesized to **increase** water **solubility** of the original DDB. In the present study, the antigenic

potential of DDB-S was examined by active systemic anaphylaxis (ASA), passive cutaneous anaphylaxis (PCA) and passive hemagglutination (PHA) tests. The exptl. groups consist of a low dosage group, a high dosage group, the group emulsified with Freund's complete adjuvant (FCA, ASA test) or an alum (PCA and PHA tests) and the macromol. conjugate group emulsified with FCA or an alum. In the ASA test, all exptl. groups showed neg. responses whereas the pos. control group given ovalbumin plus FCA showed severe anaphylactic responses. In the heterologous PCA test using mice and rats, pos. responses were not detected in any of the exptl. groups. In the PHA test, all exptl. groups showed neg. responses whereas the pos. control group given ovalbumin plus an alum showed 512-2048 PHA titers. These results demonstrated that DDB-S does not have any antigenic potential. These data can be utilized as a part of preclin. data for the development of DDB-S as an i.v. injection.

L22 ANSWER 7 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:553279 HCAPLUS
DOCUMENT NUMBER: 127:210375
TITLE: Stable pharmaceutical preparation containing human growth hormone
INVENTOR(S): Kobayashi, Hideki; Aoki, Mihoko; Uchida, Hiroshi; Kusuhara, Nobumi; Miyama, Yukio; Ito, Teruo; Fukuhara, Akira; Sato, Tsutomu
PATENT ASSIGNEE(S): Mitsui Toatsu Chemicals, Inc., Japan
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 787497	A2	19970806	EP 1997-300607	19970130
EP 787497	A3	19990414		
R: AT, BE, CH, DE, DK, FI, FR, GB, IT, LI, NL, SE				
JP 10265404	A2	19981006	JP 1997-12525	19970127
TW 509576	B	20021111	TW 1997-86101040	19970130
AU 9712433	A1	19970814	AU 1997-12433	19970131
AU 686962	B2	19980212		
US 6013773	A	20000111	US 1997-791728	19970131
CN 1165034	A	19971119	CN 1997-104964	19970202
PRIORITY APPLN. INFO.:			JP 1996-17342 A	19960202
			JP 1997-8598 A	19970121

AB The type of human growth hormone having mol. weight .apprx.20,000 (20k hGH) is stabilized and **solubilized** in water by adding a water-soluble heterocyclic compound such as creatinine, an acetyltryptophan salt, or nicotinamide, to prevent hydrophobic interactions between the protein mols. The stability of 20k hGH in solution upon thawing can be **improved** by adding a nonionic surfactant such as polysorbate 80. Stability of lyophilized 20k hGH, and its stability during reconstitution, are **improved** by adding basic amino acids and mannitol. Production of small amts. of insol. matter in 20k hGH prepns. is prevented by controlling the pH at 5-8.

L22 ANSWER 8 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:726577 HCAPLUS
DOCUMENT NUMBER: 123:84159
TITLE: 1,3,4-Oxadiazole-Containing Polymers as Electron-Injection and Blue Electroluminescent

Materials in Polymer Light-Emitting Diodes
AUTHOR(S): Pei, Q.; Yang, Y.
CORPORATE SOURCE: UNIAX Corporation, Santa Barbara, CA, 93117, USA
SOURCE: Chemistry of Materials (1995), 7(8), 1568-75
CODEN: CMATEX; ISSN: 0897-4756
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Three 1,3,4-oxadiazole-containing polymers with different **solubility** and conjugation length (repeating units of phenylene and oxadiazole) were synthesized and characterized. Among them, the polymer with the shortest conjugation length (2 phenylene and one oxadiazole rings) had the widest π-π* bandgap and was not fluorescent. As an electron-injection material, it was successfully used to **improve** the quantum efficiency of polymer light-emitting diodes (LEDs) using dialkoxy derivs. of poly(1,4-phenylenevinylene) as the electroluminescent layer and Al as the cathode. The second polymer, with an addnl. oxadiazole ring in the conjugated segment, was also an electron-injection polymer. This extra oxadiazole ring further enhanced the electron transport property and lowered the LED operating voltage **more** than the first polymer. The third 1,3,4-oxadiazole-containing polymer, with an even longer conjugation length, had strong blue fluorescence. Blue LEDs were fabricated using this polymer as the electroluminescent layer, conducting polyaniline as the hole-injection layer, Ca as the cathode, and the first 1,3,4-oxadiazole-containing polymer as the electron-injection layer. These devices emitted a bright blue light, with 4.5 V of turn-on voltage and 0.1% of external quantum efficiency.

L22 ANSWER 9 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:578894 HCAPLUS
DOCUMENT NUMBER: 122:298864
TITLE: Self-Association of Dexverapamil in Aqueous Solution
AUTHOR(S): Surakitbanharn, Yosyong; McCandless, Richard; Krzyzaniak, Joseph F.; Dannenfelser, Rose-Marie; Yalkowsky, Samuel H.
CORPORATE SOURCE: College of Pharmacy, University of Arizona, Tucson, AZ, 85721, USA
SOURCE: Journal of Pharmaceutical Sciences (1995), 84(6), 720-3
CODEN: JPMSAE; ISSN: 0022-3549
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The pKa and intrinsic **solubility** of monomeric dexverapamil were determined from its pH-**solubility** profile to be 8.90 and 6.6 + 10-5M, resp. The **solubility** of dexverapamil below pH 7.0 was higher than expected on the basis of the aforementioned values. This unusually high **solubility** is believed to be due to the self-association of cationic dexverapamil. The apparent pKa of the self-associated drug is estimated to be .apprx.7.99. The self-association of dexverapamil-HCl is supported by the fact that it is surface active and that it **increases** the **solubility** of both naphthalene and anthracene in aqueous solns. The dependence of the drug **solubility** on pH and the **solubilization** of naphthalene and anthracene as a function of ionized drug concentration suggest that the self-associated dexverapamil is a cationic dimer.

L22 ANSWER 10 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:214441 HCAPLUS
DOCUMENT NUMBER: 114:214441

TITLE: Compositions of phytic acid and pharmaceutical uses thereof
INVENTOR(S): Sawai, Kiichi; Kurono, Masayasu; Asai, Hiromoto; Mitani, Takahiko; Ninomiya, Naohisa
PATENT ASSIGNEE(S): Sanwa Kagaku Kenkyusho Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 390574	A2	19901003	EP 1990-303397	19900329
EP 390574	A3	19910717		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 02262584	A2	19901025	JP 1989-82599	19890331
US 5059594	A	19911022	US 1990-497364	19900322
PRIORITY APPLN. INFO.:			JP 1989-82599 A	19890331

AB An aqueous solution contains (a) phytic acid 1.00 mM-1.00 M; (b) Fe3+ to **increase** the **solubility** of phytic acid; (c) carboxylate ions to hasten the dissoln.; and optionally (d) other additives to enhance the bioadsorption. The molar ratio of (a):(b):(c):(d) is 10:1:1:0 to 1:12:36:200. The composition is useful for the removal of uraroma or body smell, as an antidote to the effect of alc. or drugs on the central nervous system, for the treatment of diabetes, etc., or in the inhibition of fat cells, etc. An aqueous solution containing ferric citrate 0.0604 and phytic acid 0.0302 mmol, pH 2.49 was prepared Within 10 min after anesthesia by i.p. injection of 80 mg hexobarbital/kg, the solution, at 5 mg phytic acid/kg, was administered i.p. Arousal time was reduced ≥35%, compared to a reduction of ≥30% by K phytate alone.

L22 ANSWER 11 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:30016 HCAPLUS
DOCUMENT NUMBER: 114:30016
TITLE: Aqueous **solubility** properties of a dibasic peptide-like compound
AUTHOR(S): Garren, Kevin W.; Pyter, Richard A.
CORPORATE SOURCE: Abbott Lab., North Chicago, IL, 60048, USA
SOURCE: International Journal of Pharmaceutics (1990), 63(2), 167-72
CODEN: IJPHDE; ISSN: 0378-5173
DOCUMENT TYPE: Journal
LANGUAGE: English
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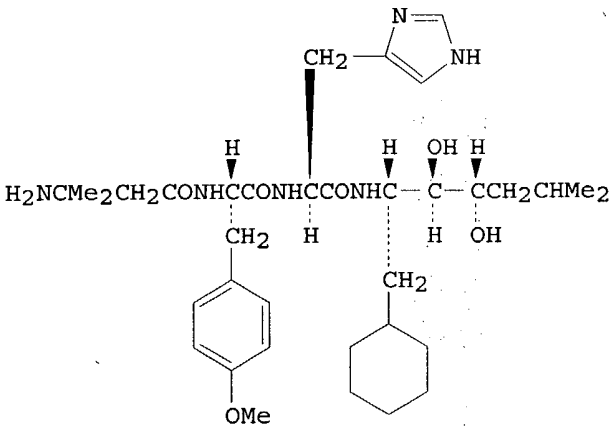

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AB The effects of pH and Cl- ion concentration on the aqueous **solubility** of a dibasic peptide-like compound (A-64662, I) were examined The **soly** .-pH profile agreed well with the theor. profile for a compound with two basic groups. Above pH 8, the **solubility** was limited by the intrinsic **solubility** of the basic form of the compound Between pH 5 and 8, the **solubility** was determined by the intrinsic **solubility** of a **monohydrochloride** salt and was highly dependent on the Cl- concentration Due to the presence of a second ionizable group, the **solubility** **increased** <pH 5. Regression analyses of the data gave ests. of 6.7 and 2.5-3.5 + 10-5 for pK1 and the **solubility** product for the **monohydrochloride** salt (Ksp1), resp. It was possible to derive equations to estimate the **solubility** of I in aqueous media of varying pH and ion concentration This study also provided results that will be helpful in understanding the **solubility** properties of other peptides that have multiple ionizable groups.

L22 ANSWER 12 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:510710 HCAPLUS
DOCUMENT NUMBER: 111:110710
TITLE: The effect of alkaloids on sugar receptors and the feeding behavior of the blowfly
AUTHOR(S): Dethier, V. G.; Bowdan, E.
CORPORATE SOURCE: Dkep. Zool., Univ. Massachusetts, Amherst, MA, 01003, USA
SOURCE: Physiological Entomology (1989), 14(2), 127-36
CODEN: PENTDE; ISSN: 0307-6962
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The deterrent effect of alkaloids on feeding by the black blowfly (Phormia regina) was tested by determining tarsal thresholds for mixts. of sucrose and alkaloids. The following alkaloids were used: atropine sulfate, berberine sulfate, quinine **monohydrochloride**, caffeine, yohimbine sulfonic ester, pilocarpine hydrochloride, coniine hydrochloride, and codeine. The same alkaloids were tested electrophysiol. on tarsal **chemoreceptors** (D hairs). Both behaviorally and electrophysiol. alkaloids reduced response to sucrose. Deterrence and peripheral inhibition could be blocked by **increasing** the concentration of sucrose. Application of kinetic analyses to the electrophysiol. data ruled out competitive, noncompetitive, and uncompetitive inhibition at receptor sites. There is no correlation of thresholds with available data on lipid **solubility** or octanol/water partition coeffs. The diverse pharmacol.

properties of alkaloids suggest that there is no uniform limiting mechanism for this multiform array of compds.

L22 ANSWER 13 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:90929 HCAPLUS
DOCUMENT NUMBER: 110:90929
TITLE: Mechanisms of interaction of amino acids with phospholipid bilayers during freezing
AUTHOR(S): Anchordoguy, Thomas; Carpenter, John F.; Loomis, Stephen H.; Crowe, John H.
CORPORATE SOURCE: Dep. Zool., Univ. California, Davis, CA, USA
SOURCE: Biochimica et Biophysica Acta (1988), 946(2), 299-306
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The ability of various amino acids to protect small unilamellar vesicles against damage during freeze/thaw was compared. Damage to liposomes frozen in liquid N2 and thawed at 20° was assessed by resonance energy transfer. Cryoprotection by numerous amino acids was compared in the presence and absence of 350 mM NaCl. The majority of amino acids with hydrocarbon side chains **increased** membrane damage during freeze/thaw regardless of the presence of salt. However, amino acids with hydrocarbon side chains of <3 C atoms in length, e.g. glycine, alanine, and 2-aminobutyric acid, were cryoprotective only in the presence of salt. NaCl is suggested to selectively **increase** the **solubility** of such amino acids, allowing them to act as cryoprotectants. In contrast, amino acids with side chains containing charged amine groups were cryoprotective regardless of the presence of salt. The degree of charge on the second amine group is shown to be important for cryoprotection by these mols. Evidence is presented that suggests an interaction between the pos. charged, second amine group of the amino acid, and the neg. charged phospholipid headgroup.

L22 ANSWER 14 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1986:141192 HCAPLUS
DOCUMENT NUMBER: 104:141192
TITLE: Analytical properties of 1,3-cyclopentanedione bis(4-methylthiosemicarbazone) **monohydrochloride**
AUTHOR(S): Ceba, Manuel Roman; Jimenez Sanchez, Juan Carlos; Galeano Diaz, Teresa
CORPORATE SOURCE: Fac. Cienc., Univ. Extremadura, Badajoz, Spain
SOURCE: Afinidad (1985), 42(398), 356-60
CODEN: AFINAE; ISSN: 0001-9704
DOCUMENT TYPE: Journal
LANGUAGE: Spanish

AB The synthesis and anal. properties of 1,3-cyclopentanedione bis(4-methylthiosemicarbazone) **monohydrochloride** (1,3-CPBMT.HCl) are described. The **solubility**, spectra, pK values, and reactions with inorg. ions are reported. To a solution of 4.29 g of methylthiosemicarbazone in 15 mL of H2O, 10 mL of EtOH and 4.5 mL of concentrated HCl, 2.0 g of 1,3-cyclopentanedione in 10 mL of EtOH is added dropwise. The mixture is evaporated on a water bath and the product is purified by several washings with EtOH (m.p. 202-4°). The **solubility** of 1,3-CPBMT.HCl was studied by W. Wittenberger's method (1950). The compound is very soluble in DMF (36.8 g/L) and H2O (18.32 g/L) and scarcely soluble in MIBK (1.47 g/L), EtOH (1.23 g/L), CHCl3 (0.32 g/L), and isoamyl alc. (0.19 g/L). The bathochromic displacement with **increasing** pH shows that in solution there are at least 3 different forms of the compound

The reactions of 1,3-CPBMT.HCl and 1,3-CPBMT with various inorg. ions were studied for possible anal. application.

L22 ANSWER 15 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1981:565024 HCAPLUS
DOCUMENT NUMBER: 95:165024
TITLE: Improved stability of methanolic Wright's stain with additive reagents
AUTHOR(S): Liao, John C.; Ponzo, John L.; Patel, Chittaranjan
CORPORATE SOURCE: Anal. Lab., Miles Lab., Inc., Elkhart, IN, 46515, USA
SOURCE: Stain Technology (1981), 56(4), 251-63
CODEN: STTEAW; ISSN: 0038-9153
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Additive reagents have been investigated to improved the stability of methanolic Wright's stain. The addition of NH2 halides, **monoalkylamine hydrochlorides**, dialkylamine hydrochlorides, or trialkylamine hydrochlorides to methanolic Wright's stain enhanced the stability of stain components in MeOH. No change in performance is observed with these additives present. Random precipitation in the stain solution was still observed with the addition of NH2 halides and **monoalkylamine hydrochlorides.** No precipitation was found in stain solns. containing hydrochlorides of most dialkylamines and trialkylamines. Of the compds. evaluated, 0.6% diethylamine.HCl added to methanolic stain solns. produced the most desirable overall results. Mechanisms of stabilization and precipitation in these stain solution are proposed.
Essentially, separation of the thiazine-eosinate ion pair through interaction with an appropriate additive **increases** stain stability. The **solubilities** of thiazine-eosinate or additive cation-eosinate ion pairs in MeOH determined the formation of precipitate in such stain solns.

L22 ANSWER 16 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1981:493351 HCAPLUS
DOCUMENT NUMBER: 95:93351
TITLE: Improved stability of methanolic Wright's stain with additive reagents
AUTHOR(S): Liao, John C.; Ponzo, John L.; Patel, Chittaranjan
CORPORATE SOURCE: Ames Res. Dev., Miles Lab., Inc., Elkhart, IN, 46515, USA
SOURCE: Stain Technology (1981), 56(4), 251-63
CODEN: STTEAW; ISSN: 0038-9153
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Additive reagents were investigated to improve the stability of methanolic Wright's stain. The addition of ammonium halides, **monoalkylamine hydrochlorides**, dialkylamine hydrochlorides or trialkylamine hydrochlorides to methanolic Wright's stain enhanced the stability of stain components in MeOH. No change in performance is observed with these additives present. Random precipitation in the stain solution was still observed with the addition of ammonium halides and **monoalkylamine hydrochlorides.** No precipitation was found in stain solns. containing hydrochlorides of most dialkylamines and trialkylamines. Of the compds. evaluated, 0.6% diethylamine HCl added to methanolic stain solns. produced the most desirable overall results. Mechanisms of stabilization and precipitation in these stain solns. are proposed. Essentially, separation of the thiazine-eosinate ion pair through interaction with an appropriate

additive **increases** stain stability. The **solubilities** of thiazine-eosinate or additive cation-eosinate ion pairs in MeOH determine the formation of ppts. in such stain solns.

L22 ANSWER 17 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1972:559957 HCAPLUS
DOCUMENT NUMBER: 77:159957
TITLE: Action mechanism of local anesthetics. 3. Correlation between lipid **solubility** and biological action of homologous local anesthetics
AUTHOR(S): Schoenenberger, H.; Petter, A.; Zwez, W.
CORPORATE SOURCE: Inst. Pharm. Lebensmittelchem., Univ. Muenchen, Munich, Fed. Rep. Ger.
SOURCE: Pharmazie (1972), 27(8), 522-3
CODEN: PHARAT; ISSN: 0031-7144
DOCUMENT TYPE: Journal; General Review
LANGUAGE: German
AB A review with 9 refs. An **increase** alkoxy chain length of cinchocaine (I) [61-12-1] homologs by -CH2 groups up to the butoxy derivative, was associated with an **increased** neg. free energy of reaction (-ΔF0), lipid **solubility**, protein binding, and an **increased** surface anesthetic activity. With the amyloxy and hexyloxy homologs of I, the lipid **solubility** and anesthetic activity decreased.

L22 ANSWER 18 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1971:91793 HCAPLUS
DOCUMENT NUMBER: 74:91793
TITLE: **Solubility** of **semicarbazide hydrochloride** in aqueous solutions of hydrochloric acid
AUTHOR(S): Korczynski, Adam; Piszczek, Longina
CORPORATE SOURCE: Politech. Gliwice, Gliwice, Pol.
SOURCE: Zeszyty Naukowe Politechniki Slaskiej, Chemia (1970), No. 53, 45-51
CODEN: ZNSCAM; ISSN: 0372-9494
DOCUMENT TYPE: Journal
LANGUAGE: Polish
AB The **solubility** of NH2CONHNH2.HCl (I) was studied in aqueous solns. contg . 38% HCl at 20-60°. In the range of stability, both temperature and HCl concentration affected the **solubility** of I. The effect of temperature was **more** pronounced in solns. of lower HCl concentration When the temperature was lowered from 70 to 30° the **solubility** of I in 5% HCl fel /l from 531 to 322 g/l., and in 20% HCl from 113 to 46 g/l.

L22 ANSWER 19 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1971:68343 HCAPLUS
DOCUMENT NUMBER: 74:68343
TITLE: Phase **solubility** analysis: alteration of a sample in situ to avoid solid solution
AUTHOR(S): Downing, George V., Jr.; Smith, George B.; White, Alan B.
CORPORATE SOURCE: Merck Sharp Dohme Res. Lab., Rahway, NJ, USA
SOURCE: Analytical Chemistry (1971), 43(2), 260-2
CODEN: ANCHAM; ISSN: 0003-2700
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A technique is described for avoiding difficulties in purity detns. by phase **solubility** anal. whereby a sample is altered in situ to avoid the formation of a solid solution of an impurity in the main component.

Thus, a solid solution of 2-(4-thiazolyl)-5-aminobenzimidazole (I) impurity in cambendazole [isopropyl 2-(4-thiazoyl)-5-benzimi-dazolylcarbamate] (II) samples was avoided by using M HCl in MeOH. Consequently, the solid phase at equilibrium is the **monohydrochloride** of II; I forms a dihydrochloride. A method is described to correct for the **solubility** product effect due to the fact that the HCl concentration is less in the systems containing **more** II sample. For essentially pure samples, the mol. weight effect due to the formation of hydrochlorides is negligible.

L22 ANSWER 20 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1971:21695 HCAPLUS
DOCUMENT NUMBER: 74:21695
TITLE: Pharmacodynamic study of derivatives of γ-(3-pyridylmethyl)theophylline
AUTHOR(S): Debaert, Michel; Laude, F.; Minard-Vaillant, Mrs.; Robelet, Alfred
CORPORATE SOURCE: Lab. Physiol. Appl. Pharmacol., Fac. Med., Lille, Fr.
SOURCE: Therapie (1970), 25(4), 683-706
CODEN: THERAP; ISSN: 0040-5957
DOCUMENT TYPE: Journal
LANGUAGE: French
GI For diagram(s), see printed CA Issue.
AB The antispasmodic and hypotensive activities of 6 theophylline derivs. with a methylpyridyl group at C-8, such as 7-(2-hydroxyethyl)-8-(3-pyridylmethyl)theophylline (mouse LD50 = 140 mg/kg, i.v.) and 7-(2,3-dihydroxypropyl)-8-(3-phyridylmethyl)-theophylline (mouse LD50 = 190 mg/kg, i.v.), were studied. With the exception of 7-(carboxymethyl)-8-(3-pyridylmethyl)-theophylline (I) (mouse LD50 = 500 mg/kg, i.v.), the derivs. had a **greater** neurotropic antispasmodic activity in the isolated guinea pig intestine than aminophylline, and a comparable musculotropic antispamodic activity and antagonistic effect against histamine-induced spasms. In the guinea pig gall bladder there was no significant difference between the antispasmodic activity of aminophylline and the derivs., with the exception of I. The antispasmodic activity of 8-(3-pyridylmethyl)theophylline (II) (mouse LD50 = 250 mg/kg, i.v.) and 7-(3-aminopropyl)-8-(3-pyridylmethyl)theophylline (mouse LD50 = 48 mg/kg, i.v.) was **greater** than or at least equal to that of aminophylline in the biliary system of guinea pigs treated with carbamylcholine. In vivo the activity of the derivs. against histamine-induced bronchospasm was less than that of aminophylline. The theophylline derivs. had a hypotensive activity in rats which was less than that of aminophylline. Although the 3-pyridylmethyl group at C-8 is favorable for antispasmodic and hypotensive activity, substituents at C-7 which **increase solubility** lessen the pharmacodynamic activity.

L22 ANSWER 21 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1968:487448 HCAPLUS
DOCUMENT NUMBER: 69:87448
TITLE: Identification of specific interactions between amino acids
AUTHOR(S): Su, S. C. K.; Shafer, J. A.
CORPORATE SOURCE: Univ. of Michigan, Ann Arbor, MI, USA
SOURCE: Journal of the American Chemical Society (1968), 90(14), 3861-4
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The interactions which determine the tertiary structure of proteins and

specific interactions between amino acids were studied. The **soly** . of common amino acids was determined in pairwise combinations. L-Arginine-HCl was effective in **increasing** the **solubility** of L-tryptophan, L-tyrosine, L-phenylalanine, and L-asparagine. L-Histidine-HCl was effective in **increasing** the **solubility** of L-tryptophan, L-tyrosine, and L-phenylalanine, while L-proline was effective in **increasing** the **solubility** of L-tryptophan and L-tyrosine. The **solubility** data were used to estimate apparent dissociation consts. for the following complexes: L-arginine-L-asparagine, 2.6M; L-arginine-L-phenylalanine, 2.2M; L-arginine-L-tryptophan, 0.80M; L-arginine-L-tyrosine, 1.3M; L-histidine-L-tryptophan, 0.61M; L-proline-L-tryptophan, 3.9M; L-proline-L-tyrosine, 7.3M.

L22 ANSWER 22 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1968:47260 HCAPLUS
DOCUMENT NUMBER: 68:47260
TITLE: Bacteriostatic and fungistatic activity of some new nitrofuran derivatives
AUTHOR(S): Jeney, Endre; Zsolnai, Tibor
CORPORATE SOURCE: Med. Univ., Debrecen, Hung.
SOURCE: Zentralblatt fuer Bakteriologie, Parasitenkunde, Infektionskrankheiten und Hygiene, Abteilung 1: Medizinisch-Hygienische Bakteriologie, Virusforschung und Parasitologie, Originale (1967), 204(3), 430-40
CODEN: ZBPHA6; ISSN: 0372-8110
DOCUMENT TYPE: Journal
LANGUAGE: German

AB The bacteriostatic and fungistatic effects of 35 new nitrofuran derivs. were investigated and compared with those of 5-nitrofurfural semicarbazone (furazin), 3-(5'-nitro-2'-furfurylideneamino)-2-oxazolidinone (Furoxone), 2-amino-5-(5'-nitro-2'-furyl)-1,3,5-thiadiazole (thiafur), 5-nitrofurfural phenylhydrazone, and 5-nitrofurfural p-nitrophenylhydrazone. 5-Nitro-2-furfurylidene derivs. of aliphatic and alicyclic ketones were **more** or less bacteriostatically effective, 2-(5-nitrofurfurylidene)cyclopentanone being an exception. 3-(5-Nitrofurfurylidene)-2-butanone (I) and 3-(5-nitrofurfurylidene)-2-pentanone (II) were the most active, being as active as furazin but not reaching the activity of Furoxone and thiafur. 2-(5-Nitrofurfurylidene)cycloheptanone was as active as Furoxone against gram-pos. staphylococci but was only half as active as furazin against gram-neg. bacteria. I, II, and 1-(5-nitrofurfurylidene)-1-phenyl-2-propanone (III) had fungistatic activity against thread-forming dermatophytes, Trichophyton gypseum and Epidermophyton. I oxime, II oxime, and III oxime were bacteriostatic as well as fungistatic. I semicarbazone, II semicarbazone, I thiosemicarbazone, and II thiosemicarbazone had no activity; I aminoquanidone hydrochloride and II aminoguanidone hydrochloride were bacteriostatically active. Condensation products of 5-nitrofurfural with rhodamines and substituted benzyl cyanides, e.g. 3-methyl-5-(5-nitrofurfurylidene)rhodanine and 4-nitro-α-(5-nitrofurfurylidene)benzyl cyanide, were inactive, as were the 5-nitrofurfural anils, e.g. N-(5-nitrofurfurylidene)aniline. 1-(5-Nitrofurfuryl)-2-(5-nitro-2-furyl)benzimidazole, which is formed by spontaneous ring closing of N,N'-bis(5-nitrofurfurylidene)-o-phenylenediamine was slightly active against gram-neg. bacteria. The antimicrobial effect of the compds. of the nitrofuran series was attributable not only to the 5-nitro-2-furyl group but also to physicochem. properties such as **solubility** protein binding, and cell permeability.

L22 ANSWER 23 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1967:498710 HCAPLUS
DOCUMENT NUMBER: 67:98710
TITLE: Relations between the physicochemical properties, reactivity, and local anesthetic activity of some procaine homologs. XX. Variation of the N-alkyl and alkylene group
AUTHOR(S): Buechi, Jakob; Perlia, Xavier; Studach, S. P.
CORPORATE SOURCE: Eidg. Tech. Hochsch., Zurich, Switz.
SOURCE: Arzneimittel-Forschung (1967), 17(8), 1012-21
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: German
GI For diagram(s), see printed CA Issue.
AB cf. CA 66: 45115v; 67: 20133g. Twenty-two 4-aminobenzoic acid dialkylamine alkyl esters were prepared by treating 4-nitrobenzoyl chloride with dialkylamino alkanol then reducing the nitro ester, or by condensing 4-nitrobenzoic acid ω-chloroalkyl ester with dialkylamine then reducing, and the local anesthetic effects were compared. **Increased** local anesthetic effects in both the alkyl and alkylene series depended on low water **solubility** of the bases, high lipid **solubility**, a low turbidity pH, and a pronounced surface activity. Differences in activity were not due to differences in the chemical reactivities of the 4-amino, carbonyl, ester, and ammonium groups but may result from the hydrophobic bonding of the alkene and alkyl groups. The local surface anesthetic effects of I, II, III, IV, and V were 2 times **greater** than those of cocaine, but these compds. were irritating and often toxic. VI, VII, and VIII were equally as active as cocaine but were also irritating. The local anesthetic effects of IX, X, III, XI, and XII, were .apprx.2 times **greater** than those of cocaine without producing irritation. The LD50 dose in white rats was 50 mg./kg. for XII and V, 75 mg./kg. for II, XI, VI, and VII, 100 mg./kg. for IX, X, III, IV, and VIII, and 125 mg./kg. for I. 32 references.

L22 ANSWER 24 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1966:63775 HCAPLUS
DOCUMENT NUMBER: 64:63775
ORIGINAL REFERENCE NO.: 64:11939h,11940a-c
TITLE: Diluent influence on liquid-liquid extraction by trilauryl-amine hydrochloride
AUTHOR(S): Mueller, W.; Duyckaerts, G.
CORPORATE SOURCE: European At. Energy Community, Ispra, Italy
SOURCE: (1965), AEC Accession No. 20039, Rept. No. EUR-2246.e, 85 pp. Avail.: AEC
From: Nucl. Sci. Abstr. 19(11), 2455(1965).
DOCUMENT TYPE: Report
LANGUAGE: English
AB cf. preceding abstract The diluent influence on liquid-liquid extraction of trivalent metals by trilaurylamine hydrochloride was investigated by means of **solubility** measurements, ir absorption spectroscopy, and by a study of the equilibrium between trilaurylamine and HCl. In general, the **solubilities** of water, HCl, and trilaurylamine chloride **increase** with **increasing** polarizability or polarity of diluents. With few exceptions, water and HCl **solubilities** are proportional to their activities in the aqueous phase, and are independent of each other. Hydration favors amine salt **solubility** Monohydrated amine hydrochloride is formed in benzene, toluene, nitrobenzene, and cyclohexane. In CCl4 and in CHCl3, the hydration of the amine salt is not complete. The anal. results are supported by ir spectroscopy. The equilibrium consts. for the formation of the amine **monohydrochloride** from

organic amine solns. and aqueous HCl **increase** with **increasing** polarizability or polarity of the diluents. The formation consts. of the amine dihydrochloride, however, decrease with **increasing** polarity (exception:nitrobenzene). Extraction of ferric or Am chloride from HCl or LiCl solns. decreases with **increasing** polarity of diluents, with the exception of nitrobenzene, whose extracting power is comparable to that of cyclohexane. Ir spectra do not reflect the interaction between the diluent and the amine salt or the extracted metal complex.

L22 ANSWER 25 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1966:25454 HCAPLUS
DOCUMENT NUMBER: 64:25454
ORIGINAL REFERENCE NO.: 64:4653c-h
TITLE: Removing sulfur from gases
PATENT ASSIGNEE(S): Societe d'Etudes et de Developement de la Catalyse Industrielle "SOCATY"
SOURCE: 22 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
NL 6501178		19650730	NL	
PRIORITY APPLN. INFO.:			FR	19640129

AB A gas containing H2S, when passed through a Fe3+ solution gives S, H2O, and Fe2+.

The solution can be reoxidized with air and reused. In the usual salt solns. the Fe2+-Fe3+ oxidation-reduction potential is high and re-oxidation is difficult and slow, but this is not so when EDTA (ethylenediaminetetraacetic acid), which is stable, cheap, and nontoxic, or similar compds. which form a Fe3+ complex are used. The tetra-Na salt of EDTA can give a 0.12-0.13M Fe3+ solution, of which 1 l. can react with 1.35-1.40 l. H2S. O-S by-products, e.g. hydrosulfites or thiosulfates are not formed. With 2 NH4+ ions present per Fe atom, 0.60-0.65M Fe3+ solns. can be obtained at similar pH, temperature, etc., with a capacity 6.75-7.0 l. H2S per l. By using the NH4+ salt of EDTA, capacities of 10-12 l. H2S per l. may be reached. NH4Cl, NH4NO3, or (NH4)2SO4, or otherwise FeSO4.(NH4)2SO4.6H2O may be added. Other suitable Fe salts are the acetate, chloride, citrate, nitrate, oxalate, sulfate, or formate. The addition of an amine salt, e.g. **monomethylamine hydrochloride**, to the Fe3+ complex of the tetra Na salt of EDTA kept at pH 7 also **increases** the **solubility** Solns. of Fe salts in the presence of EDTA and bases or NH3, or when combined as salts such as the NH4+ salt, have pH near 7, both in the Fe3+ and in the Fe2+ form, so that special corrosion-resistant construction materials need not be used. H2S and mercaptans can be simultaneously removed, the latter giving disulfides, and further treatment with soda becomes unnecessary. To remove S, the gas can be treated with the Fe3+ complex at 15-50°, but the temperature may be up to 130° if necessary to decrease the **solubility** of certain components, or otherwise be <15° but above the f.p. **Increased** temps. help the evaporation of H2O formed in the reaction. Any pressure may be used. The S flocculates and can be separated by filtration. Desulfurization and reoxidn. are equally rapid and, when air or O is present or has been added to the treated gas, can take place simultaneously. For good contact, the gas and the solution may be passed countercurrently through packed or bubble-plate columns, or liquid sprays

may be passed through the gas, depending on the S content. The flow rate must be sufficient to prevent blocking by flocculated S. The solution may be used for the desulfurization of H, CO, saturated, naphthenic, aromatic, and ethylenic hydrocarbons, and many industrial gases. For example, 2520 cc. of a 40 weight % aqueous solution of the tetra-Na salt of EDTA was placed in a flask, and 300 cc. concentrated HCl was added to bring the pH to .apprx.8. Then, 2880 cc. of an aqueous solution of FeSO4.(NH4)2SO4.6H2O with 39.6 g. Fe/l., and 920 cc. 2N Na2CO3 solution to keep pH .apprx.7 during mixing, were added while stirring. The volume was brought to 15 l. with H2O, so that the solution contained 7.6 g. Fe/l. By passing air through the solution, 85% of Fe2+ was converted to Fe3+. In a column with a 25 mm. diameter filled to a height of 1.5 m. with 5 mm. diameter cylindrical rings, the solution was allowed to flow from above at 7 l./hr., while from below N containing 250 ppm. H2S was passed through at atmospheric pressure and 35° at 250 l./hr. The exhaust gas contained <0.5 ppm. H2S. Besides EDTA, other chelating agents can be used.

L22 ANSWER 26 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1965:39587 HCAPLUS
DOCUMENT NUMBER: 62:39587
ORIGINAL REFERENCE NO.: 62:7010b-h,7011a-b
TITLE: Toxicity of heparinoids, with special reference to the precipitation of fibrinogen
AUTHOR(S): Sasaki, S.; Takemoto, T.; Oka, S.
CORPORATE SOURCE: Univ. Nagoya, Japan
SOURCE: Thrombosis et Diathesis Haemorrhagica (1964), 12(1-2), 232-61
CODEN: TDHAAT; ISSN: 0340-5338
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Partially hydrolyzed dextran, intrinsic viscosity 0.21, was further hydrolyzed by boiling in 0.1N H2SO4. The hydrolyzate was neutralized with NaOH and precipitated fractionally with Me2CO, the fractions being repeatedly precipitated to narrow the distribution of mol. weight The final precipitate was washed with alc. and Et2O, then vacuum dried. Variations in the time of acid hydrolysis were used to produce various mol. wts. Samples of dextran were sulfated with pyridine and HSO3Cl, the dextran sulfate (I) being isolated as the Na salt, which after purification showed only 1 electrophoretic component and was free of N. Mice were injected with **increasing** doses of I, and the L.D.50 was determined after 24 hrs., using the method of probits. Anticoagulant activity of I was determined in vitro by the U.S.P. method, using heparin as the standard, and ox plasma to replace sheep plasma. Human albumin, γ-globulin, and fibrinogen were obtained by Cohn fractionation, the proteins were dissolved in 0.066M phosphate buffer (pH 7) to make 0.7% solns., and centrifuged. Supernatants were collected for immediate use, the concns. being determined by the micro-Kjeldahl method. I, on addition to fibrinogen solution, gave a turbidity, and the turbid solution was serially diluted Turbidity measurements showed a linearr elation between absorbance and concentration, of precipitate Maximum turbidity was seen in 3 min. with I of 32,000 mol. weight, and in 30 min. with mol. weight 8600, after which time the turbidity remained constant A deposit was formed in 60 min., which could be resuspended to initial turbidity by shaking. In subsequent tests, 3 ml. of 0.0002-2.0% I in phosphate buffer (pH 7) was added to 3-ml. aliquots of 0.7% fibrinogen in the same buffer, mixing being accomplished by transfer. After 60 min. at 20°, the tubes were shaken and transmission determined on the Beckman spectrophotometer at 650

mμ and 20°, using a fibrinogen-buffer blank. Animals were injected intravenously with I solns. and autopsied within 1 hr. of death. Tissue blocks were fixed in Carney's fluid for 1-2 days, then stained with Toluidine Blue or hematoxylin-eosin. **Increasing** amts. of I were added to a given quantity of citrated human plasma. The quantity of precipitate **increased** with **increased** I, up to a point, after which addnl. I **increased** the **solubility** of the precipitate The same I was added to plasma components. Albumin and γ-globulin did not, but fibrinogen did form a precipitate, the turbidity thus being caused by the precipitation of fibrinogen. If the mol. weight of I was **increased**, an **increase** amount of fibrinogen precipitated The relation of L.D.50 to turbidity of the various I was demonstrated math. and graphically, and these calcns. plus in vitro and pathol. observations indicated that the toxicity of I was due to precipitation of fibrinogen. Adult rabbits and puppies were given intravenous injections of I of various mol. wts., all having 18% S content. Puppies, given 1 injection of 0.7 g. I (mol. weight 200,000)/kg., died immediately, microscopy of fixed sections showing innumerable metachromatic emboli in capillaries of the lung, brain, and viscera. I, 0.1 g. of mol. weight 22,000, was injected daily into rabbits, causing death on days 3 or 4, and autopsy showed widespread changes, primarily from intravascular precipitate, with capillary occlusion. I, 0.1 g. of mol. weight 13,000, injected into rabbits daily, caused death on days 3 or 4, the changes being less dramatic, and predominantly degenerative damage to proximal renal tubular epithelium, with an amorphous eosinophilic substance in the tubules and Bowman's capsules. I, of mol. weight 6500, given 0.1 g./kg./day for 1 week did not cause death in rabbits, although upon sacrifice some osmotic nephrotic changes were seen. I, 0.1 g. of mol. weight 5900/kg./day, was given for 7 days, with no evidence of pathology seen after sacrifice. A rough parallelism between pathology and mol. weight was seen in the rabbit. Math. determination showed mol. wts. 6700-5300 to be the most suitable for clin. use; therefore I of mol. weight 6700, 18.2% S, was prepared Anticoagulant activity was determined to be 6 units/mg. (heparin units), the L.D.50 (mouse) was 3630 mg./kg., 380 mg. did not injure a 4-kg. monkey, and in vivo 300 mg. of I was as effective as 50 mg. heparin. Ten thrombotic human patients were treated by intermittent injections of 400 mg. I, so that clotting time was maintained at twice normal. Treatment was from 6 to 40 days. Transient diarrhea was seen in 2, and **increased** loss of hair in 4 cases. Thrombocytopenia was found in all 10 cases. Platelet counts decreased gradually to 1/3 normal by day 13, and remained constant following subsequent injections, to return to normal by 15 days after termination of injections of I. No changes were seen in red and white cell counts, hemoglobin, or liver and kidney functions. In all cases, clin. improvement of the thrombotic symptoms was observed. 55 references.

L22 ANSWER 27 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1962:33593 HCAPLUS
DOCUMENT NUMBER: 56:33593
ORIGINAL REFERENCE NO.: 56:6408i,6409a-b
TITLE: Effect of monuron and of related compounds on the growth of seedling peas
AUTHOR(S): Hassall, K. A.
CORPORATE SOURCE: Univ. Reading, Engl.
SOURCE: Journal of Experimental Botany (1961), 12, 47-55
CODEN: JEBOA6; ISSN: 0022-0957

DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Pea shoots grown in phosphate buffer were no **more** sensitive to monuron (I) applied continuously than were roots, but they were **more** readily damaged when high I concns. were applied for short periods of time. Neither roots nor shoots were **more** sensitive to I in light than in darkness. The damage caused by high I concentration was much greater under conditions of high metabolic activity. The toxicities of alkyl or aryl substituted ureas and thioureas were closely related to their **solubility** in H2O. I probably disrupts an integrating surface rather than acting upon specific active groups of enzymes.

L22 ANSWER 28 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1949:52429 HCAPLUS
DOCUMENT NUMBER: 43:52429
ORIGINAL REFERENCE NO.: 43:9374g-i,9375a
TITLE: Amino compounds with local anesthetic properties. VII. 4-Diethylaminobenzylphenylalkyl amines
AUTHOR(S): Niinobe, Shinkichi
SOURCE: Yakugaku Zasshi (1949), 69, 37-9
CODEN: YKKZAJ; ISSN: 0031-6903
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB p-Diethylaminobenzaldehyde and phenylalkylamines were condensed by heating in toluene, and the products reduced with Na and EtOH. Et2NC6H4CH2NHCH2Ph.2HCl (I), fine needles, m. 205.7°; Et2NC6H4CH2NHCHMePh.2HCl (II), needles, m. 205-7°; Et2NC6H4CH2NHCHEtPh.2HCl (III), needles, m. 203°; Et2NC6H4CH2NHCHMeCH2Ph.2HCl (IV), columns, m. 215-16°; Et2NC6H4CH2NHCH2CH2CH2Ph.2HCl (V), fine needles, m. 202°. **Solubility** products in H2O at pH 4.7-5.3 are high, but the compds. are difficultly soluble in EtOH. Local anesthetic properties were 5 times **greater** than that of cocaine in IV, 2.5 times in V; toxic action was less than 1/2 that of cocaine, except for V. Because of the strong irritant action of these products on mucous membrane, their use is not practical. The **monohydrochlorides** are less irritant, but they have the defect of lower **solubility** in H2O.

L22 ANSWER 29 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1942:35652 HCAPLUS
DOCUMENT NUMBER: 36:35652
ORIGINAL REFERENCE NO.: 36:5550f-i,5551a-d
TITLE: Pharmacological effects of **monocaine hydrochloride**
AUTHOR(S): Schamp, J. R.; Schamp, H. M.; Tainter, M. L.
SOURCE: Anesthesiology (1942), 3, 295-302,398-413
CODEN: ANESAV; ISSN: 0003-3022
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C. A. 35, 8102.7; 36, 1092.4. The **solubility** of monocaine (I), an isomer of procaine (II), is limited; only about a 2.6% solution can be made in water and a 1.5% solution in physiol. NaCl solution at room temperature The pH of a 1% solution was 5.59, as measured with a glass electrode. Solns. of I decompose slowly on exposure to light and air and during pressure sterilization. However, addition of NaHSO3 produces adequate stability. As a surface anesthetic, I was found to be twice as efficient as II on the frog skin, when tested by the Turck method, and of about equal potency by instillation in rabbit conjunctiva. The motor nerve fibers in the frog sciatic nerve were paralyzed equally well by I and II. Block of sensory

fibers after injection into tissues around the eyes of rabbits was produced by lower concns. of II than of I but the **relative** potency was reversed when adrenaline (III) was added to the solns. Sensory fibers in rabbit skin were paralyzed by slightly lower concns. of I than II, but in human skin, in the presence of III, the anesthetic efficiencies of both agents were the same. The effects of I on the frog sciatic nerve were not always fully reversible; this indicates a direct injurious action on nerve tissue. Similarly, the subcutaneous tissues of rats were irritated **more** by I than II, according to the trypan blue test and the presence of inflammatory changes in the tissues. When injected under standard conditions, 1.4% I caused sloughs in the skin in one half the animals as compared with 3.4% II required for the same degree of local irritant action. Hence, I was definitely **more** injurious for tissues than was II. The systemic toxicity of I was about 40% greater than that of II, as indicated by fatal doses injected intravenously in rats and mice and intraperitoneally in rats. In mice, this toxicity ratio was reversed for subcutaneous and intraperitoneal administrations; this possibly indicates some lack of absorption from these 2 regions in this species. In cats under pentobarbital anesthesia, the fatal dose of I was 35.1 mg. per kg., as compared with 30.9 mg. per kg. for II, a difference which the standard errors showed not to be reliable. When artificial respiration was maintained in the cats, the fatal dose of I was **increased** to 111 mg. per kg. and that of II to 454 mg. per kg.; this indicates that I was about 4 times as toxic for the cardiovascular system as was II. Neither I nor II caused pressor actions due to peripheral vasoconstriction when injected intravenously in rabbits and cats. I and II did not **increase** the pressor responses to III and thus there was no demonstrable synergism with or **increase** in effects between these anesthetics and III. There was the same lack of pressor and synergistic responses in perfused blood vessels where all except peripheral effects were eliminated. Indirect tests for enhanced vasocontrictor responses to I and III, consisting of comparing the incidence of tissue sloughs under quant. conditions, and the interference with absorption of strychnine from subcutaneous tissues, failed to give evidence of any heightening of III effects in the presence of I. These results taken together indicate that the local anesthetic efficiency of I is similar to that of II, as is also the systemic toxicity, except for a greater cardiovascular paralyzing action of I. They also fail to substantiate current claims that I is a pressor agent, or that it enhances the actions of III. Since I is definitely **more** irritating to tissues than II, it lacks the advantages which would justify its selection over II as a local anesthetic for injection purposes.

L22 ANSWER 30 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1941:25464 HCAPLUS
DOCUMENT NUMBER: 35:25464
ORIGINAL REFERENCE NO.: 35:4056a-b
TITLE: p-Aminodimethylaniline **monohydrochloride** as an indicator of microbial action on fats
AUTHOR(S): Castell, C. H.
SOURCE: Stain Tech. (1941), 16, 33-6
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The flooding of plates containing fat emulsion agar inoculated with various types of microorganisms with this dye frequently results in marked color changes in the fat globules. These colors result from the **increased solubility** in fat and fat acids of this dye as it becomes oxidized. A table is included showing the colors in globules of oil that were inoculated with 39 pure cultures of bacteria.

L22 ANSWER 31 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1940:48354 HCAPLUS
DOCUMENT NUMBER: 34:48354
ORIGINAL REFERENCE NO.: 34:7405c-i,7406a-b
TITLE: Sulfanilylguanidine: a chemotherapeutic agent for intestinal infections
AUTHOR(S): Marshall, E. K., Jr.; Bratton, A. Calvin; White, H. J.; Litchfield, J. T., Jr.
SOURCE: Bulletin of the Johns Hopkins Hospital (1940), 57, 163-88
CODEN: JHHBAI; ISSN: 0097-1383
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Several sulfanilamide derivs. were found to be H2O-soluble and quite poorly absorbed from the gastrointestinal tract. Such compds. make possible a new approach to the chemotherapy of intestinal infections. The use of intestinal antiseptics heretofore has depended upon low water **soly**. to avoid absorption. The idea of a drug which is fairly water-soluble and therapeutically active but not absorbed from the intestine presents a new principle in the use of the new bacterial chemotherapeutic agents; the fundamental principle involved is the achievement of a high concentration of the drug in the intestine and a low concentration in the blood and tissues, a situation somewhat analogous to the use of sulfanilamide derivs. as urinary antiseptics. Pharmacological and therapeutic studies are reported on sulfanilylguanidine (I), which is the most bactericidal of the compds. studied. The authors describe a method for the preparation of N4-acetylsulfanilylguanidine, from which I is obtained by acid hydrolysis. The pure, crystalline compound obtained has a H2O **solubility** of 220 mg./100 cc.; the solution so obtained has pH 6.9, and is practically tasteless. The preparation and properties of the **monohydrochloride**, dihydrochloride and picrate of I are described. p-NH2C6H4SO2NHC-(:NH)NH2 and p-NH2C6H4SO2N:C(NH2)2 are suggested as the most probable structural formulas for I; it is further suggested that these structures may represent resonance isomers. I can be determined in blood, urine, spinal fluid and tissues by the colorimetric method employed for sulfanilamide derivs. (C. A. 33, 5017.4; 34, 5172.6). Toxicity expts. are difficult because of low rate of intestinal absorption after oral administration, and limited **solubility** in parenteral administration. Dogs tolerate the maximum possible intravenous injection of 0.2 g./kg., and can be injected intraperitoneally with large quantities of I dissolved in olive oil. I is less toxic for dogs by this route than sulfapyridine. Chronic toxicity per os is low in mice and dogs, but higher in rabbits, which acetylate I and deposit the acetylated derivative in the renal tubules, causing diminished kidney function and delayed excretion of I. Conjugation of I occurs in the mouse, rabbit and man, but not in the dog; in the rabbit the conjugated form is N4-acetylsulfanilylguanidine. Absorption and excretion of I was studied by giving mice a solution of I in acacia; the absorption is demonstrated to be slower than that of sulfapyridine. From the peritoneal cavity, I is absorbed readily; it penetrates all tissues rapidly with the exception of brain and passes into the spinal fluid much **more** slowly than sulfanilamide and sulfapyridine. After intravenous injection, 95% of I is excreted in the urine within 24 hrs. The renal clearance of I in a dog averaged 20 cc./min. as compared with 5.5 cc./min. for the clearance of sulfanilamide in the same animal. I is probably absorbed **more** readily from the small than from the large intestine. Its effectiveness against exptl. mouse pneumonia is comparable with that of sulfapyridine; it is somewhat less effective than sulfanilamide against exptl. beta-hemolytic streptococcus infections. In vitro tests with a number

of different bacterial species show that I is at least as effective as sulfanilamide. The nos. of coliform organisms in the intestinal contents of mice can be reduced markedly by placing the animals on a diet containing 1% of I.

L22 ANSWER 32 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1937:18613 HCAPLUS
DOCUMENT NUMBER: 31:18613
ORIGINAL REFERENCE NO.: 31:2602c-i,2603a
TITLE: Spontaneous resolution of racemic histidine **monohydrochloride**
AUTHOR(S): Duschinsky, Robert
SOURCE: Festschrift Emil C. Barell (1936) 375-93
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C. A. 28, 2004.9. The **solubility** isotherms obtained with a mixture of active and racemic histidine-HCl (I) show that the inactive substance is a true racemate between 20° and 40°. Between 40° and 55° there is a transition point where the racemate is transformed into a conglomerate of antipodes. The strong tendency of active and racemic I to give supersatd. solns. makes possible the realization of stable states far removed from true equilibrium conditions. It is thus possible to crystallize an optical isomer from a solution with the opposite rotatory power. Conditions favoring spontaneous resolution are discussed and it has been found that the best results are obtained by beginning crystallization in the region of stability of the active compound and finishing in that of the racemate. A solution of 30 g. of racemic I (containing 15.6% Cl) was completely dissolved in 20 cc. of hot H2O and cooled to about 56°. After the addition of a crystal of l- and another of d-I the solution was heated to 58° to start the crystallization After cooling to 55° the material was filtered on a funnel at 55° and washed 3 times with 30 cc. of boiling alc. and then with 50 cc. anhydrous Et2O. Drying in vacuo at room temperature gave 12 g. dl-I, C6H9N3O2.HCl.H2O, which was transformed, on standing for 4 days in the open, to C6H9N3O2.HCl.2H2O. A mixture containing 20 g. of l-I, [α]D20 -39°, and 42.3 g. of dl-I was taken up in 58 g. H2O and stirred steadily at 55° for 1 hr. The inactive solution was filtered off through a Buchner funnel at 55°, washed with 5 cc. of 40% alc. and with 96% alc. and Et2O, yielding 21 g. of l-I, [α]D20 -37°. Concentration of the mother liquor in vacuo gave 41 g. of dl-I. The spontaneous resolution of dl-I was carried out by dissolving 63 g. of l-I and 135 g. of dl-I in 300 cc. of distilled H2O at 65°. After cooling to 48° a crystal of l-I was added and the solution was cooled, with continuous stirring, to 20° in 15 min. The material was filtered and washed with 40 cc. of 40% alc. and 20 cc. of 96% alc. The washings were collected separately. The residue, dried at 100°, gave 83 g. of l-I, [α]D20 -36°, corresponding to 77 g. of pure compound, [α]D20 -39°, a gain of 14 g. of l-I. The wash alc. yielded 5 g. of dl-I which was added to the filtrate. This aqueous filtrate containing 97-100 g. of racemate and 14 g. of d-I was **increased** by the addition of 49 g. of d-I, 35-8 g. of racemate and sufficient H2O to 498 g. This mixture was identical with the above starting mixture but with reversed rotation. Repetition of the crystallization procedure gave 83 g. of d-I [α]D20 36° corresponding to a gain of 28 g. The filtrate contained an excess of 14 g. of l-I. Each repetition with the same mother liquor resulted in the gain of 28 g. of active material. On heating 50 g. of active I and 50 g. H2O at 6-8 kg. pressure for 3 hrs. in a small autoclave an inactive yellow solution was obtained which, on the addition of 200 cc. alc.,

gave 51 g. (94%) of racemate. The combination of these procedures for obtaining the 2 antipodes in quant. yields and of racemization of the optical isomers with yields exceeding 90% permits the almost quant. transformation of d-I into the biologically important l-antipode.

L22 ANSWER 33 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1931:26956 HCAPLUS
DOCUMENT NUMBER: 25:26956
ORIGINAL REFERENCE NO.: 25:2973h-i,2974a-d
TITLE: The behavior of polypeptides, containing lysine with substitution in α- and υ-position, toward N alkali, erepsin and trypsin
AUTHOR(S): Abderhalden, Emil; Schweitzer, Friedrich
SOURCE: Fermentforschung (1931), 12, 350-75
CODEN: FEFOAG; ISSN: 0367-2034
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB The υ-NH2 group of the lysine component of proteins is generally believed to be unsubstituted, although no convincing proof has yet been offered. This paper deals with the enzymic cleavage of lysine peptides in which the α- or the υ-NH2, or both, occur in acid amide linkage. The α-lysine peptides were obtained by the usual peptide synthesis, starting with υ-benzoyllysine in which the υ-NH2 was already occupied by Bz and thus excluded from the coupling reaction. Similarly, the υ-peptides were made from α-methyl- lysine in which only the υ-NH2 was free to react. The α,υ-diaminoacyllysines were obtained directly from unsubstituted lysine. υ-Benzoyllysine (I), which served as the starting material, was prepared from benzoylpiperidine by the v. Braun method (C. A. 3, 1273). I → υ-N-benzoyl-α-(dl-α-bromopropionyl)-dl-lysine (II), m. 129-30°, → υ-N-benzoyl-α-dl-alanyl-dl-lysine (III), m. 240°, υ-N-benzoyl-α-(N-benzoyl-dl- alanyl)-dl-lysine, m. 145-6°. I → υ-N-benzoyl-α-(dl-α-bromoisocaproyl)-dl-lysine (IV), m. 148-50°, → υ-N-benzoyl-α-dl-leucyl-dl-lysine, m. 232-3°, → υ-N-benzoyl-α- (N-benzoyl-dl-leucyl)-dl-lysine, m. 155-6°. IV + PhCH2NH2 → υ-N-benzoyl-α-(N-benzyl-dl-leucyl)-dl-lysine, m. 190-1°. I → υ-N-benzoyl-α-(dl-α-bromocaproyl)-dl- lysine, m. 140°, → υ-N-benzoyl-α-dl-norleucyl-dl-lysine, m. 251-2°. III → υ-N- benzoyl-α-(dl-α-bromoisocaproyl-dl-alanyl)-dl-lysine, m. 154-5°, → υ-N-benzoyl-α- (dl-leucyl-dl-alanyl)-dl-lysine (V), decomps. 90°. I → α,υ-dibenzoyl-dl-lysine, m. 146-7°, → I, m. 252°, → II, hence this method is unsuitable for the preparation of α-benzoyllysine. dl-υ-Benzoylamino-α-bromocaproic acid (v. Braun) + MeNH2 → υ-N-benzoyl-α-methyl-dl-lysine, m. 233-4° → α-N-methyl-dl-lysine HCl salt (VI), m. 244-5° (HI salt, m. 239-41° (decomposition)) → υ-(dl-α-bromopropionyl)-α-N- methyl-dl-lysine → υ-dl-alanyl-α-N-methyl-dl-lysine (VII) m. 115α. VI → υ-(dl-α- bromoisocaproyl)-α-N-methyl-dl-lysine, m. 119-21°, → υ-dl-leucyl-α-N-methyl-dl-lysine (VIII), decomps. 120α. dl-Lysine mono-HCl salt (IX), m. 235-6°, is **more** easily handled than the di-HCl salt because of its lower **solubility** and **greater** readiness of crystallization IX → α,υ-di(dl-bromopropionyl)-dl-lysine → α,υ-di(dl-alanyl)-dl-lysine (X). IX →

α,υ-di(dl-bromoisocaproyl)-dl-lysine, m. 93-4°,
→ α,υ-di(dl-leucyl)-dl-lysine (XI), m. 130°.
Erepsin attacked III, V and X, the extent of cleavage indicating that only the α-linkage was broken. Trypsin-kinase attacked V and XI, the latter only to 25%. Here again it appears that only the α-peptide linkage is broken. The 10.7% cleavage of VIII is considered questionable. All of these derivs. were hydrolyzed **more** or less by N alkali at 37°. The important observation is that the υ-peptide linkage of lysine polypeptides is resistant to enzymes. A typical illustration is the ereptic cleavage of III and non-cleavage of VII. These observations support the view that the lysine component of proteins is linked only through its α-NH2.

L22 ANSWER 34 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1920:12600 HCAPLUS
DOCUMENT NUMBER: 14:12600
ORIGINAL REFERENCE NO.: 14:2336b-f
TITLE: Pelletierine and methylpelletierine
AUTHOR(S): Tanret, Georges
SOURCE: Compt. rend. (1920), 170, 1118-20
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Issue is taken with Hess and Eichel (Ber. 1917-8), who propose to strike out the term isopelletierine and use pelletierine (A) for the optically inactive form of A called isopelletierine (B) by Tanret, as they did not isolate optically active A. Its existence is proved by the following additional facts: The sulfate (C), (C8H15ON)2H2SO4.3H2O, m. 133° when anhydrous, [α]D -30.3° in H2O; yield, 0.7-1.0 g. per kg. bark. Hydrochloride, m. about 145°, [α]D -41.2°; hydrobromide, m. about 137°, [α]D -32.5°; nitrate, m. 82-5°, [α]D -34.5°; picrate, m. 131-2°; chloroplatinate, m. 214-6°; silicotungstate, has 2H2O of crystallization; in Et2O A gives [α]D -31.1°, in H2O -27 8°; acetylpelletierine, C10H17O2N, b40 205-10°, [α]D + 32.6°; benzoylpelletierine, cannot be boiled without decomposition, [α]D 18.7°; saponification of the acyl derivs. with H2SO4 yields the racemic form, B. **Semicarbazone hydrochloride**, m. 168-70°, [α]D -10.8°. H. and E.'s inability to obtain optically active A was due to the sensitiveness of A to heat and to alkali, both of which cause rapid racemization. Even C loses in optical activity in H2O at 100°, although stable in excess dilute H2SO4. A even racemizes when distilled in vacuo in a current of H; after 2 distns. at 52 mm. it is inactive. Nor did H. and E. obtain T.'s active methylpelletierine (D). D, b45 106-8°; [α]D 27.7, [α]D 24.1° in H2O, c = 10, and is not affected by successive distns. or treatment with dilute alkali. D dissolves in H2O in all proportions, but below 35.5° in concns. above 50% the **solubility increases** with the temperature, while in concns. below 50% it diminishes with **increasing** temperature Hydrochloride, m. 168-70°, [α]D 41.2°; hydrobromide, m. 165-7°, [α]D 33.5°; sulfate, [α]D 38°; picrate, m. 157-9°; chloroplatinate, m. 206-8°; the bark contains about 0.03 g. D per kg.

L22 ANSWER 35 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1920:11747 HCAPLUS
DOCUMENT NUMBER: 14:11747
ORIGINAL REFERENCE NO.: 14:2197e-i,2198a-i,2199a
TITLE: Some derivatives of 4(5)-methyl-5(4)-aminomethylimidazole arylated on the amino group, and

the synthesis of β-p-hydroxyphenyl-3,4(5)-imidazolylethylamine
AUTHOR(S): Gerngross, Otto
SOURCE: Ber. (1919), 52B, 2304-18
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C. A. 6, 1297. (In the following, R=N:CH.NH.CMe.C-.) 4(5)-Methylimidazolyl-5((4)-methylaniline((A),RCH2NHPh, is obtained in 0.35 g. yield when 0.5 g. of the anil RCH:NPh (if **greater** amts. are used the yield falls very much) in 7.5 cc. of gently boiling, C5H5N-free iso-AmOH is treated in 7 portions with 0.5 g. clean Na in a H atmospheric, quickly cooled, dissolved in 27.5 cc. of N HCl, evaporated in vacuo, freed from NaCl by repeated extraction with absolute alc. and evaporation, suspended in a little absolute alc. and cautiously treated with Et2O; the dihydrochloride thus obtained seps. in 4-cornered platelets from alc., turns green 175°, sinters 195°, m. 199°, crysts. from H2O in 4-sided prisms, from MeOH + AcOEt or Et2O in hone-shaped plate-lets, decomps. slightly and becomes green in the air. Free base, 4- and 6-sided plates from alc., m. 181°, soluble in 7 parts boiling alc., in 20 parts boiling Me2CO from which it seps. in moss-like crystals easily soluble in C5H5N and seps. in platelets on addition of H2O; its solns. are strongly alkaline to litmus; with diazobenzenesulfonic acid in soda it gives the characteristic blood-red color; it is easily soluble in dilute weak acids but insol. in alkalies; 0.6 g. in 5.2 cc. of cold 5 % NaOH slowly treated with 0.74 cc. BzCl in 16 cc. Et2O and 8 cc. of 10% NaOH gives 0.6 g. of the benzanilide, RCH2NBzPh, quadratic plates from 75% alc., m. 203°, 4-sided prisms from AcOEt, forms solns. strongly alkaline to litmus, easily soluble in N HCl, insol. in NaOH, dissolves transiently in 30 parts of 20% HCl but the solution soon deposits the hydrochloride in stout prisms, m. 230°; only after long heating is the Bz group split off; it does not couple with diazobenzenesulfonic acid either in soda or NaOH. A is **more** conveniently prepared by rapidly treating 5.3 g. dry RCH2Cl.-HCl in 3 cc. MeOH at -20° with 5.75 cc. PhNH2 (2 mols.), letting stand 0.5 hr., boiling 3 hrs. under a reflux, evaporating in vacuo, dissolving in 10.5 cc. H2O and slowly adding 56 cc. of N NaOH; the crude product (3.5 g., dried at 100°), is boiled 0.5 hr. with 24 parts Me2CO, which dissolves out the A, 2.7 g. of which are obtained; there remains undissolved 0.6 g. N-[di-4(5)-methylimidazolyl-5(4)-methyl]aniline, (RCH2)2NPh, which is obtained in 23% yield, with but little A, when 3 g. RCH2Cl.HCl in 15 cc. MeOH at -18° is allowed to stand with 1.62 cc. PhNH2: (1 mol.) in 3 cc. MeOH for some time and then boiled 4 hrs.; it is soluble in about 35 parts boiling alc. and seps. in needles, m. 197-8°, is strongly alkaline to litmus, gives a blood-red color with diazobenzenesulfonic acid in soda, is insol. in NaOH, is not attacked by BzCl and NaOH in the cold. 4(5)-Methylimidazolyl-5(4)-methyl-β-phenylethylamine, RCH2NHCH2CH2Ph, is obtained as the dipicrate in 7.5 g. yield from 3.34 g. RCH2Cl.HCl in 18 cc. MeOH added in the course of 45 min. to 8.1 cc. (somewhat **more** than 3 mols.) PhCH2CH2NH2 in 75 cc. H2O and 5 cc. MeOH at 1°, allowed to stand some time, boiled 1.25 hrs., evaporated in vacuo, stirred with a little absolute alc., cooled in ice, filtered from the excess of PhCH2CH2NH2.HCl (which is washed with 3:1 Me2CO-EtOH), treated with 15.6 g. picric acid in 150 cc. absolute alc. and allowed to stand overnight; the picrate is soluble in 60-70 parts boiling Me2CO and seps. in prisms, sinters 204°, m. 209°, crysts. from (CO2Et)2 in thick plates; dihydrochloride (2 g. from 9.4 g. of the picrate boiled with 30 parts of HCl (d. 1.19)), somewhat hygroscopic leaves, m. 249° (foaming), 6-sided plates from EtOH-Et2O;

chloraurate, yellow crystals, foams 212°. From the Me2CO mother liquors of the dipicrate can be obtained a small amount of [di-4(5)-methylimidazolyl-5(4)-methyl-β-phenylethyl]amine tripicrate, which is the chief product (about 4.3 g., with 1.2 g. of the above dipicrate) when 3.34 g. RCH2Cl.HCl is treated with 5.4 cc. (2 mols.) PhCH2CH2NH2; it sinters 160°, M. 174°, seps. from AcOH in yellow crystals, from Me2CO-RtOH in 4-sided tables, is soluble in about to parts boiling Me2CO; the hydrochloride, wart-like crystals from EtOH-Et2O is very hygroscopic; chloroplatinate, 2C18H23N5.3H2PtCl6, hygroscopic plates, blackens above 200°, does not m. 270°, N-4(5)-Methylimidazolyl-5(4)-methyl-p-phenylenediamine trihydrochloride, RCH2NHC6H4NH2.3HCl, obtained in 1.5 g. yield from 3 g. RCH2Cl.HCl and 1.94 g. p-C6H4(NH2)2 and separated from the excess of the latter by its **greater solubility** in cold concentrated HCl, precipitated from alc. by saturation with HCl, seps. from the alc. solution containing a few drops dilute HCl on addition of Et2O or Me2CO in 4-sided Plates, m. 257°; dipicrate, yellow spears, m. 215-6°, soluble in about 60 parts hot H2O and seps. in needles, while from absolute alc. and AcOH it crysts. in red plates. When 8.2 g. crystallized histamine (best obtained by treating the di-HO salt in H2O with soda, evaporating to dryness and freeing completely from NaCl and excess of Na2CO3 by repeatedly dissolving in absolute alc., adding Et2O and filtering), which has been dried to constant weight at 80° in vacuo, is heated 10 hrs. at 100° with 4.6 g. p-HOC6H4CH2CH2Cl in 40 cc. dry MeOH, acidified with alc. HCl, evaporated in vacuo, saturated at 0° in 60 cc. absolute alc. with HCl, filtered from the histamine-HCl after long standing in the ice chest, again evaporated in vacuo and saturated in 20 cc. alc. with HCl, filtered, evaporated in vacuo after addition of H2O to remove HCl and treated in 100 cc. hot H2O with 13.4 g. picric acid in 900 cc. boiling H2O, and the precipitate is digested with cold MeOH there is obtained 9 g. of p-hydroxyphenylethyl]-[imidazolylethyl]amine dipicrate, orange-red needles, m. 201.5°, soluble in 120 parts hot EtOH, 60 parts boiling MeOH, 30 parts boiling Me2CO, seps. from AcOH in light orange-red needles; when digested with 15 parts cold 5 N HCl it gives the dihydrochloride, only slightly hygroscopic crystals from alc. containing a little HCl, m. 199-200°, easily soluble in H2O with neutral reaction; treated in H2O with excess of NH4OH, evaporated in vacuo and treated with a drop of H2O, it gives the **monohydrochloride** in 4-sided platelets, m. 1930; its solns. are alkaline; it is also obtained from the free base in 1 mol. HCl. Both HCl salts have a pronounced bitter taste. Free base, from the HCl salt in H2O containing a little H2SO4, shaken with Ag2SO4, freed from Ag with HCl and from H2SO4 with Ba(OH)2 and evaporated in vacua at 40° to incipient turbidity, 4-sided microprisms, m. 156°, soluble in 6 parts boiling alc., seps. in plates on very cautious addition of petr. ether, reacts strongly alkaline, is easily soluble in acids and alkalies, gives, like the HCl salt, with diazobenzenesulfonic acid in alkali a blood-red color and with Millon reagent the usual red color; the HCl salt in concentrated solution gives with FeCl3 a not very characteristic brown-greenish color.

L22 ANSWER 36 OF 36 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1909:6183 HCAPLUS
DOCUMENT NUMBER: 3:6183
ORIGINAL REFERENCE NO.: 3:1148h-i,1149a-c
TITLE: Cinchonamine and Certain other Rare Alkaloids
AUTHOR(S): Howard, B. F.; Chick, O.
SOURCE: Journal of the Society of Chemical Industry, London (1909), 28, 53-7
CODEN: JSCIAN; ISSN: 0368-4075

DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB It was shown in a previous paper that the **insolubility** of cinchonamine nitrate could be used for determining nitrates gravimetrically (Ibid., 24, 1281). Further experiments showed that the method can be used in many cases. For the analysis of KNO3 a sol containing 0.6 g. of the hydrochloride for every 0.1 g. of KNO3 and a large excess of HCl must be added, the mixture must be allowed to stand for 24 h. and not **more** than 100 cc. wash H2O must be used for every g. of precipitated nitrate. The method is as accurate as the nitrometer method. It may be employed for the estimation of all nitrates except those of the metals which give insol. chlorides or oxychlorides. The limit of precipitation of HNO3 in glacial AcOH is 1 in 500, while in H2O the limit is 1 in 100000. Cinchonamine does not contain MeO. Its formula, C10H24ON2, was corroborated by the analysis of the chlorplatinate. Quinicine was made by Pasteur's method, but could not be made to crystallize. It contains 1 MeO and forms a crystalline a acid tartrate, a neutral oxalate, 2C20H24N2O.C2H2O4, 9H2O, and a chlorplatinate, but, contrary to Hesse's statement, the 2 sulphates, the hydriodide and the thiocyanate are amorphous. Cinchonicine (by Pasteur's method) forms a crystalline acid tartrate containing 1 H2O and a crystalline oxalate, 2C19H22N2O.C2H2O4, 7H2O. Concusconine, as shown by its chlorplatinate, is C23H26N2O4, and contains 2 MeO. The only chlorplatinate obtainable from cupreine is C19H22N2O2.H2PtCl6,H2O. Leger's basic chlorplatinate could not be obtained. Contrary to former statements, cupreinesulphate contains no H2O. Hesse's statement of cupreine bisulphate containing 1 H2O was corroborated. Cupreine tetrasulphate, C19H22N2O2.2H2SO4, deliquescent crystals. Cupreine **monohydrochloride** contains 1 H2O. Cupreine dihydrochloride contains no H2O. The [α]D of cupreine in EtOH is -163°, 45' (Leger, -175°, 5'). Cupreine contains no MeO.

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NEWS 2		"Ask CAS" for self-help around the clock
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NEWS 4	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS 5	SEP 01	New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
NEWS 6	SEP 27	STANDARDS will no longer be available on STN
NEWS 7	SEP 27	SWETSCAN will no longer be available on STN
NEWS 8	OCT 28	KOREAPAT now available on STN
NEWS 9	NOV 18	Current-awareness alerts, saved answer sets, and current search transcripts to be affected by CERAB, COMPUAB, ELCOM, and SOLIDSTATE reloads

NEWS EXPRESS	OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
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FILE 'HOME' ENTERED AT 00:35:43 ON 24 NOV 2004

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 00:35:48 ON 24 NOV 2004
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 22 NOV 2004 HIGHEST RN 786612-66-6
DICTIONARY FILE UPDATES: 22 NOV 2004 HIGHEST RN 786612-66-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

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h eb c g cg b cg eb

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> file medline, biosis, caplus, embase

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.42	0.63

FILE 'MEDLINE' ENTERED AT 00:36:08 ON 24 NOV 2004

FILE 'BIOSIS' ENTERED AT 00:36:08 ON 24 NOV 2004
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FILE 'CAPLUS' ENTERED AT 00:36:08 ON 24 NOV 2004
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FILE 'EMBASE' ENTERED AT 00:36:08 ON 24 NOV 2004
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=> s semi-hydrochloride? or semihydrochloride?
L1 9 SEMI-HYDROCHLORIDE? OR SEMIHYDROCHLORIDE?

=> s l1 and solub?
L2 3 L1 AND SOLUB?

=> s mono-hydrochloride?
L3 47 MONO-HYDROCHLORIDE?

=> s l3 and solub?
L4 3 L3 AND SOLUB?

=> s l4 and l2
L5 0 L4 AND L2

=> s l2 and review
L6 0 L2 AND REVIEW

=> s l4 and review
L7 0 L4 AND REVIEW

=> d l2, cbib abs, 1-3

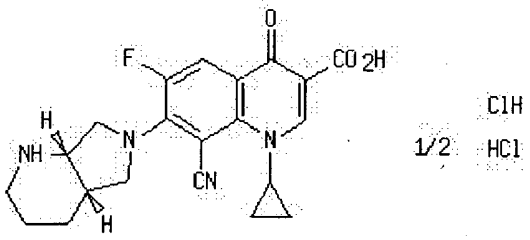
L2 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

Citing References

2000:366037 Document No. 133:4647 **Semihydrochloride** of 8-cyano-1-cyclopropyl-7-(1S,6S-2,8-diazabicyclo[4.3.0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid. Himmler, Thomas; Rast, Hubert (Bayer A.-G., Germany). Ger. Offen. DE 19854357 A1 20000531, 16 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1998-19854357 19981125.

GI

h eb c g cg b cg eb



I

AB The title compd. (I), useful as a medical and veterinary bactericide, shows good water **soly**. (19 wt.%). I is produced by reaction of 7-halo-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid with (1S,6S)-2,8-diazabicyclo[4.3.0]nonane in the presence of a base in one of the following diluents: (a) a C≥4 aliph. alc., (b) a mixt. of a C>3 alc. with the polar aprotic diluent, N-methylpyrrolidone; (c) a mixt. of n-PrOH with DMF. I (m. 278-280°) is characterized by its powder x-ray diffractogram, differential thermogram, and IR spectrum.

L2 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

CAPLUS References

1936:47953 Document No. 30:47953 Original Reference No. 30:6375g-i,6376a-e γ-Triazines. XXXII. Catalytic hydrogenations in the group of γ-triazines. 1. Passage from methyldihydroxytriazine to the so-called trigenic acid of Liebig and Wohler. Ostrogovich, Adriano; Ostrogovich, Giorgio Gazzetta Chimica Italiana, 66, 48-57 (Unavailable) 1936. CODEN: GCITA9. ISSN: 0016-5603.

GI For diagram(s), see printed CA Issue.

AB cf. O. and Galea, C. A. 30, 469.7. It was shown earlier (cf. O., Gazz. chim. ital. 25, ii, 442(1895)) that methyldihydroxytriazine (I) is not hydrogenated by such simple means as Zn + AcOH or Zn + HCl. The present work shows that by the catalytic action of Pt black, I absorbs rapidly and quantitatively, at room temp. and ordinary pressure, 1 mole of H. Preliminary expts. indicate that this method is applicable to other γ-triazines. Hydrogenation was carried out in a Stark app. (cf. C. A. 7, 3555) in a modified form which is described and illustrated. The following percentage yields in the various media at room temp. were obtained: water 93-4; dil. HCl (aq. I.HCl), 94; dil. H2SO4 (aq. I.H2SO4), 93-4; glacial AcOH, 84. Absorption of H was about twice as rapid in acid as in neutral medium. The preferable method is to hydrogenate I.HCl, particularly since the best synthesis of I gives I.HCl. Al-Hg and Na-Hg in water at room temp. gave yields of 90-2 and 80%, resp.; Sn and dil. HCl at 60° gave a 90% yield. The product is in all cases cycloethylidenebiuret (methyldihydroxytriazidine), OC.NH.CO.NH.CMeH.NH (II), the formation of which is analogous to that of dihydroresorcinol from resorcinol, dihydroorcinol from orcinol and dihydrouracils from uracils. II m. 272-3° (decompn.) with evolution of collidine (III); its **soly**. in boiling water is 5.5 g. per 100 cc., in water at 20° it is 1 g. per 100 cc. In the prepn. of II catalytically in glacial AcOH, the initial product, which can be isolated, is a monoacetate, C4H7O2N3.C2H4O2, of II, hydrolyzes in water immediately to II. There were also prepd. a **semihydrochloride**, (C4H7O2N3)2.HCl.3H2O; a semichloroaurate, (C4H7O2N3)2.AuCl3H.2H2O; and a semipicrate, C4H7O2N3.C6H3O7N3. No sulfate could be prepd. Contrary to L. and W., the Ag salt contains 1 H2O of crystn. With Nessler reagent or with Hg(OAc)2 and an alkali, II ppts. a mercuric salt (IV), HN.CO.N(HgOH).CO.N(HgOH).CMeH.2H2O or HN.CO.N(HgOH).CMeH.N(HgOH).CO.2H2O, not altered by hot 10% aq. KOH, does not turn yellow. Alk. salts of II

h eb c g cg b cg eb

could not be isolated because of their tendency to hydrolyze and to absorb CO2. With Ac2O and a little concd. H2SO4, II forms a di-Ac deriv., probably AcN.CO.NH.CO.NAc.CMeH (V), m. 171-2°, does not evolve III when heated to a high temp.; heated with alc. NH3 in a sealed tube, or with 10% aq. KOH it reverts to II. In accordance with this, with Nessler reagent V forms IV only slowly, i. e., after preliminary hydrolysis. Herzig in 1882 concluded that the trigenic acid (IV) of Liebig and Wohler (Ann. 59, 296(1846)) was II, but the properties of II as prepd. in the present work differed in some ways. Thus II does not have an acid taste nor an acid reaction in water. To settle the problem, IV was prepd. by the directions of L. and W., and all its phys. and chem. properties were found to be identical to those of II, including those of the various derivs.

L2 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

Cited References

1911:16581 Document No. 5:16581 Original Reference No. 5:2830c-g
Derivatives of p-Aminophenylarsenious Oxide. Bertheim, A. (Chem. Dept., Frankfort a/M). Ber., 44, 1070-5 (Unavailable) 1911.

AB cf. C. A., 4, 1752. p-Aminophenylarsenious chloride hydrochloride, Cl2AsC6H4NH2.HCl, is obtained in a state of purity by dissolving p-aminophenylarsenious oxide in 2 N HCl and adding the liquid to well cooled, conc. HCl; needles, m. 139-40°. It is acid towards "Congo" and when heated decomp. into PhNH2 and AsCl3. Yield, 49.2%. p-Aminopheny-larsenious bromide hydrobromide, Br2AsC6H4NH2.HBr, is prepared like the chloride, which it resembles; crystallin, m. 134°. Yield, 95.6%. p-Aminophenylarsenious iodide hydriodide, I2AsC6H4NH2.HI, is obtained like the preceding compds., but it is more convenient to prepare it by the action of HI (d. 1.7) on arsanilic acid; intensely yellow, crystallin powder, darkens 90°, then decomp. p-Acetaminophenylarsenious oxide, AcNHC6H4AsO, is prepared from arsanilic acid, KI and SO2; crystallin, darkens about 280°, m. about 288-9° (decomp.). It is sparingly **sol**. Yield, about 33%. A second, hydrated modification is obtained by the interaction of p-aminophenylarsenious oxide and Ac2O; crystals with 1 H2O, m. 100°, when again heated, m. 271°. It is readily **sol**. Yield, about 76%. With I, in presence of AcONa, it is oxidized to acetoarsanilic acid. The anhydrous form may be converted into the hydrated modification, but the reverse change could not be realized. Acetaminophenylarsenious chloride **semihydrochloride**, (AcNHC6H4AsCl2)2.HCl, is prepared by the interaction of acetoarsanilic acid and PCl3, in AcOEt; warty aggregates of opaque crystals, m. 137° (gas evol.). Yield, about 60-70° of the acid. With aq. NaOH it gives p-acetaminophenylarsenious oxide. In H2O its reaction is acid.

```
=> s hydrochloride?
L8      233908 HYDROCHLORIDE?

=> s l9 and sol?
L9 NOT FOUND
The L-number entered could not be found.  To see the definition
of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s l8 and sol?
L9       70193 L8 AND SOL?

=> s l9 and review
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h eb c g cg b cg eb

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L10         313 L9 AND REVIEW

=> s semihydrochloride?
L11           9 SEMIHYDROCHLORIDE?

=> s l11 and solubility
L12           2 L11 AND SOLUBILITY

=> s l12 and l8
L13           1 L12 AND L8

=> d l13, cbib abs, 1

L13  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2004 ACS on STN
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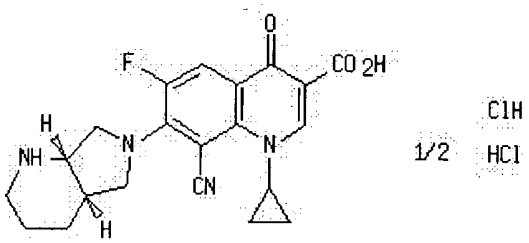
2000:366037 Document No. 133:4647 **Semihydrochloride** of 8-cyano-1-cyclopropyl-7-(1S,6S-2,8-diazabicyclo[4.3.0]nonan-8-yl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid. Himmler, Thomas; Rast, Hubert (Bayer A.-G., Germany). Ger. Offen. DE 19854357 A1 20000531, 16 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1998-19854357 19981125.

GI



I

AB The title compd. (I), useful as a medical and veterinary bactericide, shows good water **soly**. (19 wt.%). I is produced by reaction of 7-halo-8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid with (1S,6S)-2,8-diazabicyclo[4.3.0]nonane in the presence of a base in one of the following diluents: (a) a C≥4 aliph. alc., (b) a mixt. of a C>3 alc. with the polar aprotic diluent, N-methylpyrrolidone; (c) a mixt. of n-PrOH with DMF. I (m. 278-280°) is characterized by its powder x-ray diffractogram, differential thermogram, and IR spectrum.

```
=> d l12, ibib abs, 102
      2 ANSWERS ARE AVAILABLE.  SPECIFIED ANSWER NUMBER EXCEEDS ANSWER SET SIZE
The answer numbers requested are not in the answer set.
ENTER ANSWER NUMBER OR RANGE (1):0
NUMBERS IN RANGE MUST BE GREATER THAN ZERO.
An answer number must be a positive number.
ENTER ANSWER NUMBER OR RANGE (1):0
NUMBERS IN RANGE MUST BE GREATER THAN ZERO.
An answer number must be a positive number.
ENTER ANSWER NUMBER OR RANGE (1):end

=> d his

     (FILE 'HOME' ENTERED AT 00:35:43 ON 24 NOV 2004)

     FILE 'REGISTRY' ENTERED AT 00:35:48 ON 24 NOV 2004
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h eb c g cg b cg eb

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     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 00:36:08 ON 24 NOV 2004
L1             9 S SEMI-HYDROCHLORIDE? OR SEMIHYDROCHLORIDE?
L2             3 S L1 AND SOLUB?
L3            47 S MONO-HYDROCHLORIDE?
L4             3 S L3 AND SOLUB?
L5             0 S L4 AND L2
L6             0 S L2 AND REVIEW
L7             0 S L4 AND REVIEW
L8        233908 S HYDROCHLORIDE?
L9         70193 S L8 AND SOL?
L10          313 S L9 AND REVIEW
L11            9 S SEMIHYDROCHLORIDE?
L12            2 S L11 AND SOLUBILITY
L13            1 S L12 AND L8

=> s l12 not l13
L14            1 L12 NOT L13

=> d l14, cbib abs, 1

L14  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2004 ACS on STN
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Show References

1936:47953 Document No. 30:47953 Original Reference No. 30:6375g-i,6376a-e

γ-Triazines. XXXII. Catalytic hydrogenations in the group of γ-triazines. 1. Passage from methyldihydroxytriazine to the so-called trigenic acid of Liebig and Wohler. Ostrogovich, Adriano; Ostrogovich, Giorgio Gazzetta Chimica Italiana, 66, 48-57 (Unavailable) 1936. CODEN: GCITA9. ISSN: 0016-5603.

GI For diagram(s), see printed CA Issue.

AB cf. O. and Galea, C. A. 30, 469.7. It was shown earlier (cf. O., Gazz. chim. ital. 25, ii, 442(1895)) that methyldihydroxytriazine (I) is not hydrogenated by such simple means as Zn + AcOH or Zn + HCl. The present work shows that by the catalytic action of Pt black, I absorbs rapidly and quantitatively, at room temp. and ordinary pressure, 1 mole of H. Preliminary expts. indicate that this method is applicable to other γ-triazines. Hydrogenation was carried out in a Stark app. (cf. C. A. 7, 3555) in a modified form which is described and illustrated. The following percentage yields in the various media at room temp. were obtained: water 93-4; dil. HCl (aq. I.HCl), 94; dil. H2SO4 (aq. I.H2SO4), 93-4; glacial AcOH, 84. Absorption of H was about twice as rapid in acid as in neutral medium. The preferable method is to hydrogenate I.HCl, particularly since the best synthesis of I gives I.HCl. Al-Hg and Na-Hg in water at room temp. gave yields of 90-2 and 80%, resp.; Sn and dil. HCl at 60° gave a 90% yield. The product is in all cases cycloethylidenebiuret (methyldihydroxytriazidine), OC.NH.CO.NH.CMeH.NH (II), the formation of which is analogous to that of dihydroresorcinol from resorcinol, dihydroorcinol from orcinol and dihydrouracils from uracils. II m. 272-3° (decompn.) with evolution of collidine (III); its **soly.** in boiling water is 5.5 g. per 100 cc., in water at 20° it is 1 g. per 100 cc. In the prepn. of II catalytically in glacial AcOH, the initial product, which can be isolated, is a monoacetate, C4H7O2N3.C2H4O2, of II, hydrolyzes in water immediately to II. There were also prepd. a **semihydrochloride**, (C4H7O2N3)2.HCl.3H2O; a semichloroaurate, (C4H7O2N3)2.AuCl3H.2H2O; and a semipicrate, C4H7O2N3.C6H3O7N3. No sulfate could be prepd. Contrary to L. and W., the Ag salt contains 1 H2O of crystn. With Nessler reagent or with Hg(OAc)2 and an alkali, II ppts. a mercuric salt (IV),

h eb c g cg b cg eb

HN.CO.N(HgOH).CO.N(HgOH).CMeH.2H2O or HN.CO.N(HgOH).CMeH.N(HgOH).CO.2H2O, not altered by hot 10% aq. KOH, does not turn yellow. Alk. salts of II could not be isolated because of their tendency to hydrolyze and to absorb CO2. With Ac2O and a little concd. H2SO4, II forms a di-Ac deriv., probably AcN.CO.NH.CO.NAc.CMeH (V), m. 171-2°, does not evolve III when heated to a high temp.; heated with alc. NH3 in a sealed tube, or with 10% aq. KOH it reverts to II. In accordance with this, with Nessler reagent V forms IV only slowly, i. e., after preliminary hydrolysis. Herzig in 1882 concluded that the trigenic acid (IV) of Liebig and Wohler (Ann. 59, 296(1846)) was II, but the properties of II as prepd. in the present work differed in some ways. Thus II does not have an acid taste nor an acid reaction in water. To settle the problem, IV was prepd. by the directions of L. and W., and all its phys. and chem. properties were found to be identical to those of II, including those of the various derivs.

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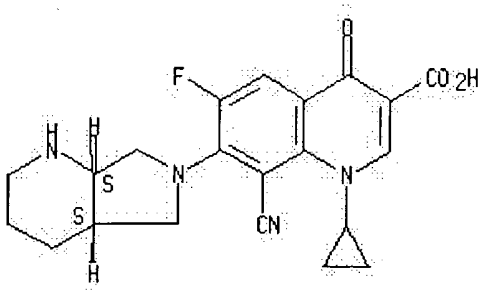

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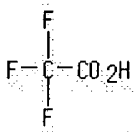
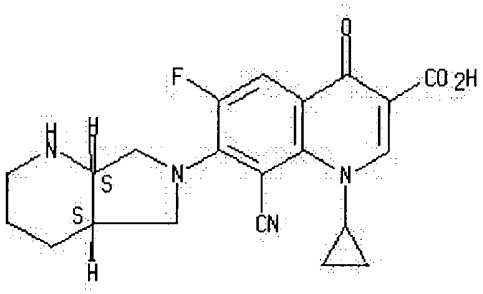


RN 195532-58-2 HCAPLUS
CN 3-Quinolinecarboxylic acid, 8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-7-(octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl)-4-oxo-, monosodium salt, (4aS-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Na

=> d his

(FILE 'HOME' ENTERED AT 19:16:30 ON 24 NOV 2004)

FILE 'REGISTRY' ENTERED AT 19:16:39 ON 24 NOV 2004
L1 STRUCTURE UPLOADED
L2 0 S L1
L3 0 S L1 FULL
L4 STRUCTURE UPLOADED
L5 0 S L4
L6 7 S L4 FULL

FILE 'HCAPLUS' ENTERED AT 19:21:40 ON 24 NOV 2004
L7 12 S L6
L8 6 S L7 AND HIMMLER, T?/AU

=> s l7 not l8

h eb c g cg b cg eb

```
L9             6 L7 NOT L8

=> s l9 and rast, h?/au
            90 RAST, H?/AU
L10          0 L9 AND RAST, H?/AU

=> d l9, ibib abs hitstr, 1-9

L9   ANSWER 1 OF 6  HCAPLUS  COPYRIGHT 2004 ACS on STN
```

Full Text | Citing References

ACCESSION NUMBER: 2004:800774 HCAPLUS
DOCUMENT NUMBER: 141:282840
TITLE: Controlled-release drug delivery system containing saccharose acetate isobutyrate (SAIB)
INVENTOR(S): Fraatz, Kristine; Mertin, Dirk; Heep, Iris
PATENT ASSIGNEE(S): Bayer Healthcare AG, Germany
SOURCE: Ger. Offen., 8 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10312346	A1	20040930	DE 2003-10312346	20030320
WO 2004082658	A1	20040930	WO 2004-EP2318	20040306

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DE 2003-10312346 A 20030320

AB The invention concerns controlled-release drug delivery systems that include (a) a drug; (b) saccharose acetate isobutyrate (SAIB); (c) glycerinformal, isopropylidene glycerol or their mixt. as solvent. A cosolvent can be added; they are selected from the group of ethanol, n-butanol and benzyl alc. Thus a formulation contained (wt./wt.%): SAIB 40; pradofloxacin 3; n-butanol 3; ethanol 5; 1N HCl 1.7; glycerinformal to 100.

IT **195532-12-8**, Pradofloxacin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (controlled release drug delivery system contg. saccharose acetate isobutyrate (SAIB))
RN 195532-12-8 HCAPLUS
CN 3-Quinolinecarboxylic acid, 8-cyano-1-cyclopropyl-6-fluoro-1,4-dihydro-7-[(4aS,7aS)-octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl]-4-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.